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Osler, Master of an Era

IAGO GALDSTON*

IT is a hundred years since Osler was born, and thirty since he died. It is fitting therefore that we should, so to say, conjure up his person, and reflect upon it. That is one warrant for the anniversary, that it provides the occasion for a reassessment of values. But to reassess Osler is rather difficult. The judgment of his contemporaries, their fulsome praise of him and the honors they conferred upon him both living and dead crowd too large upon our awareness to permit the exercise of independent judgment. The assessments of those who knew him in the flesh are intimidating both by their unison and unequivocal temper. For the re-evaluation of Osler there is wanted a longer perspective, knowledge of the intimate particulars of Osler's life, and such free play of judgment and opinion as only the stage disencumbered of those whose feelings might be hurt can afford.

If, however, we may not at this time reassess Osler, we can at least speculate about him, and for speculation two among several possible themes are particularly enticing: these are Osler the man, and Osler the physician.

On the score of the first, that is Osler the man, speculation must needs be doubly speculative. We are limited to reflect on what we *might* possibly know did we but first know the essential and missing facts about his inner and more intimate life. Cushing's *The Life of Sir William Osler,*[1] for all its fifteen hundred pages, beshrouds rather than reveals the intimate man.

That biography is full of stir and bustle. So much is told of what the man *did,* and so little of what he felt, and of his doings only those which decorum would countenance. This is not to take Cushing to task. We are told that Lady Osler, not unlike Lady Burton, "edited" the biography of her famous spouse.[2] Whatever the reason therefor, the facts are that we know far too little of Osler's inner life to make the man entirely understandable.

And Osler the man is a provocative challenge to those who would uncover the mainsprings of man's actions. Osler's life is uncommonly full of puzzlements and paradoxes. It is certain that he was kindhearted and sin-

* The New York Academy of Medicine.

[1] Cushing, Harvey. *The life of Sir William Osler.* Oxford, 1925, 2 vols.

[2] "She also guided H. C. in matters of taste and there were evidently serious differences from time to time as to what could or could not be included. Lady Osler occasionally protested about the inclusion of details that she regarded as essentially private, and she at times abused 'Harvey' in her frank, good-natured way about using her letters and leaving so little to the imagination." (Fulton, John F. *Harvey Cushing; a biography.* Springfield, Ill., 1946, p. 462.)

cere, without guile or pomposity. Yet he was also a confirmed practical joker, and the practical joke is ever an act of *cruel* aggression.

It is affirmed that Osler never made an enemy of any normal man, and that in itself renders him suspect. The Greeks banished Aristides because he was too good, and critical reason is always alerted by the presence of uncommon virtue. Osler was a most generous man, yet at times his generosity is embarrassing to contemplate, as when it embraces some too obscure functionary. No doubt it *was* praiseworthy. Yet that is its very disturbing aspect: so much that Osler did was praiseworthy!

The son of a minister, Osler first studied for the ministry, then turned to medicine. Three men were the heroes of his youth and life: William Arthur Johnson, James Bovell, and Robert Palmer Howard. To them he dedicated his *principles.*[3] Johnson was a clergyman-schoolmaster with a taste for natural history. When bored or troubled Osler would scribble "James Bovell." Osler was devoted to his mother, and she lived to the age of 100. His father appears to have had the lesser influence upon his life.

What bearing may all of this have upon his marriage late in life (*aet.* 42) to the widow of his friend; upon his "sadistic humor"; upon his reprobate *alter ego,* Egerton Y. Davis; upon his enormous drive, upon his addiction to arithmetical statements, upon his rôle as a collector and cataloguer?

We can only raise these questions, believing them valid. We cannot for want of particular knowledge venture further. Yet it is to be hoped that before too long the wanted particular knowledge will be made available so that we may really know what manner of man was this Osler. One thing seems certain, in the presence of such knowledge Osler will become a more familiar, but not a less esteemed personage, for whatever the mainspring of his action, he was in effect a good man whom many loved, and to whom countless were beholden in countless ways.

On Osler the physician we may speculate with greater facility and assurance. On this score most of the pertinent facts are known. The speculation lies in how the facts are summated. There are three phases to Osler the physician; the practitioner, the teacher, and the author of the *Principles.* They are in effect but three facets of his medical personage. We can hardly presume to comment on Osler the practitioner, beyond repeating what is already well known, that his contemporaries considered him an excellent diagnostician. He appears to have been less acclaimed as a therapist, though this may be due to the fact that serving as a diagnostician-consultant, therapy was left to the consulting physician. Osler was not in any sense a thera-

[3] Osler, William. *The principles and practice of medicine.* New York, 1892.

peutic nihilist, but he had little use for the motley array of drugs and remedies common in his apprentice years.

Osler the teacher, and the author of the *Principles,* interests us most. In these he was the master of an era which crowned an epoch in medical history. It is not likely that any shall inherit his crown (as none has to this day) for the epoch of which he was master came to an end even before his death in 1919. Osler was the last of the great physicians whose competence and preëminence rested solidly on a foundation of thorough training in, and knowledge of, classical pathology.[4] This is not to deny that there are not even now excellent physicians well trained in pathology, nor is it intended to disparage the value of the study of pathology in the training of the physician. It is intended rather to affirm that Osler was preëminently a pathologist, and that he visualized, taught, and wrote medicine, in the perspective of pathology. He could hardly have done otherwise, for that in essence was the nature of his training and the substance of his experience. Pathology was the foundation of the medicine he learned and the medicine he taught.

In his *Principles,* published in 1892, Osler summed up that vast accumulation of pathological insight and knowledge to which Vesalius, Malpighi, and Leeuwenhoek contributed the alphabet, and Morgagni, Bichat, Rokitansky, and Virchow, the grammar and syntax of the anatomical language of disease. That summation was further enriched by the knowledge derived from the labors of Pasteur, Koch, and their associates. Written in clear language, offering the data of original experience, expounding in an orderly fashion the definition, history, distribution, etiology, symptoms, morbid anatomy, diagnosis, prophylaxis, and treatment of each disease, classed and subjoined according to the so-called anatomical systems, the *Principles* did indeed seem the *non plus ultra* of medical textbooks. The work was a great success, and has gone through sixteen editions. In each successive edition the text was modified to bring it abreast of medical progress, but the fundamental pattern of the book remained unchanged. There appeared to be no warrant for change, for the *Principles* mirrored and illuminated the best in the theory and practice of contemporary medicine. Other textbooks on medicine were much like Osler's, not because they copied his, but because there appeared to be no other way for the effective presentation of the lessons learned.

[4] "Indeed the cultivation of pathology in their early professional years was, from the beginning of the nineteenth century on, characteristic of physicians who rose to high eminence." (Welch, William H. A great physician and medical humanist. A review of Harvey Cushing's *Life of Sir William Osler.* Separately printed by permission of *The Saturday Review of Literature,* November, 1925, p. 11.)

Osler crowned an era that came to an end during his life, and his *Principles* is the last epitome of that era. It is doubtful, however, that Osler ever appreciated all this. Welch, who was Osler's contemporary and collaborator, and who like Osler *began* as a pathologist, did appreciate the passing of the era. Osler, however, appeared to believe, tacitly rather than affirmingly, that medicine would progress quite along the line, or pattern, of past progress, and quite in the way it was reflected in his textbook. Different sections might be altered, enlarged, or abridged, but the skeleton, the schema, would endure. Osler was not alone in this belief; he was but one among the very vast majority. That majority, though somewhat reduced, still obtains today.

Major Greenwood is of the opinion that Osler was impervious to intellectual experience: "After he left Canada [he was then 35 years old], Osler's intellectual growth was in extent rather than in depth; he covered a wider and wider surface, but he struck no roots."[5] Osler's framework of medical thought and concept was little affected by the rise of the sciences of endocrinology, nutrition and psychiatry. The data of these specialties, in so far as they could be *written into* his text, found place in his *Principles. But their effect upon his outlook and understanding was additive rather than alterative.*

"Osler was a pathologist of the old fashioned type."[6] Precisely what this implies can be gathered clearly and succinctly from the memorable address delivered by the archpriest of pathologists, Rudolf Virchow, at the XIth International Congress of Medicine, held in Rome in 1894. Virchow spoke on Morgagni and the Anatomical Idea. The burden of his thesis was the following. Before Morgagni and ever since the days of Hippocrates, the principal concern of medicine was to define the nature of disease, the *Natur der Krankheit.* Morgagni, who approached the study of disease as an anatomist, was not concerned with the *nature* of disease but with its *locus.* The title of his great work was *De sedibus morborum.* The great service of Morgagni, according to Virchow, was to demonstrate *ad oculos,* that "there is no such thing as a sick body, altered in each of its parts. This is the sense of the words *'sedes morbi'* which Morgagni set forth as the quintessence of his discovery."[7]

What Morgagni had initiated was thereafter developed by others, and

[5] Greenwood, Major. *The medical dictator and other biographical studies.* London, 1936. "Osler of 'Osler,'" p. 153.

[6] Greenwood, *ibid.,* p. 151.

[7] Virchow, Rudolf Ludwig Karl. *Morgagni und der anatomische Gedanke* [Morgagni and the anatomical idea]. An address delivered at the XIth International Congress of Medicine in Rome, March 30, 1894. Berlin, 1894, p. 21.

the advance of medicine can be summed up in the saga of the search for the seat of disease, that is "from organs to tissues, from tissues to cells." The practice of medicine followed suit, adopting the principle of "local treatment" and applying it in ever more refined and particular ways to the innermost parts of the body heretofore considered unreachable. With the advance of the science of cellular pathology both pharmacology and surgery became more local in their purview and objectives.

Ubi est morbus, Virchow affirmed, is the query with which the study and examination both of the living patient, and the dead body must be initiated. In this concept of specificity, initiated with the quest for the *sedes morborum,* and expanded to embrace *local,* i.e., specific diagnoses and specific therapy, Virchow saw the apogee of modern medicine. The future could not but follow the tangent drawn from Morgagni to Virchow! Virchow ended his peroration with the following words: "It is this thought [that of the seat of disease] which dominates modern physiology and pathology. Whether you chose to trace it, with me, back to the cells, or formulate it otherwise, it will assuredly remain the thought of the future, and this future will count its inception from the days of Morgagni. To him the honor!"[8]

Involved but not too sharply revealed in the citations given above is Virchow's triumphant rejection of humoral pathology. To demonstrate the seat of the disease was in his judgment tantamount to disallowing, discrediting, and disproving humoral pathology, with its ideas on *dyscrasia,* and its concept of the sick man. There is no such thing as a sick body, Virchow said. "In every sick person there remains a considerable, yes as a rule, the greater portion of healthy being, and that which is sick or even dead, constitutes but a part of the body."[9]

Time has proved Virchow to have erred. He was proved wrong less in what he affirmed than in what he denied. For it has been shown that there is both "the seat of disease" and "the body sick in all its parts." This demonstration is the achievement of the *new era,* of which nutrition, endocrinology, and psychiatry are most representative. Virchow and Osler, however, belong to the old era.

Osler, we are told by Welch, often applied to himself Gibbon's admission that "he had drawn a high prize in the lottery of life." And for himself Welch affirms that "one cannot fail to be impressed with the almost perfect adaptation of his [Osler's] talents and temperament to the accidents and circumstances of his life. . . ." Osler did draw a high prize in the lot-

[8] Virchow, *op. cit.,* p. 23.

[9] Virchow, *op. cit.,* p. 21.

tery of life. He was born in the right time, and with the right gifts for his time. His great credit lies in the skill and perseverance with which he adapted his talents and temperament to the accidents and circumstances of his time. Born in any age, it seems certain that Osler would have "charmed" his contemporaries. But, whether he also would have been *the* Osler of "Osler" seems rather doubtful.

One can fancy Francis of Assisi a saint in every age, Abelard a great inquisitor unbounden by time or clime, and Leonardo exercising his genius no less on the atom than on aught else. But Osler seems fixed to the period which he adorned. He cannot be transposed.

I cannot quite agree that "in a few generations Osler will be as soundly forgotten as Thomas Watson or even William Jenner." I rather believe that the future will deal kindlier with him, and that it will assess him, less the fine intellect and more the man who to the best of his appreciable abilities embodied, applied, and transmitted all that is finest and best in the Doctor.

Osler on Miner's Phthisis

GEORGE ROSEN

WILLIAM OSLER'S deep and abiding interest in pulmonary disease is well documented. Evidence of this tendency may already be found during his early Montreal years. At this period in the young professor's career his concern with pathology outweighed most other interests. A report "On the Pathology of Miner's Lung" presented by Osler in 1875 to the Medico-Chirurgical Society reflects this preoccupation, but is also noteworthy in several other respects. Although a minor, but significant contribution to our knowledge of an important occupational disease, this report clearly reveals some of the basic qualities which characterized Osler throughout his career.

For many years it was denied that the black lung of miners was the direct consequence of their occupation.[1] It took decades of investigation and controversy to establish the fact that by inhaling a dust-laden atmosphere the pulmonary organs of miners became impregnated with dust. Not until the extraneous origin of miner's black lung had been irrefutably established was a solution of the problems of pulmonary anthracosis possible. In 1860 light was thrown upon the entire subject of miner's lung by the observations of two investigators working independently of each other. Both of these men, T. B. Peacock and Ludwig Traube, isolated particulate matter from the lungs of workers employed in dusty atmospheres. Peacock discovered in the incinerated lungs of buhrstone cutters gritty particles apparently identical with the stone upon which the workers had been employed. In the lungs of a patient who for more than ten years had worked in an atmosphere filled with coal dust, Traube found black particles which were coal. In the wake of his report appeared a number of important contributions confirming his findings and adding further information to the existing body of knowledge concerning miners' lungs. Among these researches of the sixties are to be found the beginnings of experimental investigation in the field of pulmonary dust disease. In 1862 Alexandre Villaret produced the first definite experimental proof that coal dust can be inhaled into the lungs. Further experimental studies were carried out by Lewin (1863), Rosenthal (1866), Knauff (1867), and Slavjansky (1869).

This is the background against which Osler's studies on the pathology

[1] Rosen, George. *The history of miners' diseases. A medical and social interpretation.* New York, Schuman's, 1943, pp. 244–403.

of miner's lung must be considered. Altogether he published four reports dealing with the subject. The first of these, to which reference has already been made, appeared in 1875 in the *Canada Medical and Surgical Journal.*[2] Osler based this report on the case of a man who had been his patient, as well as on other specimens from the museum of McGill College illustrating the pathology of lung pigmentation. The man whose lungs Osler described had died of malignant smallpox after an illness of five days.

On postmortem examination, four hours after death, "both lungs presented over their whole surface a uniform deep blue-black colour; so general was it, that not a trace of the natural hue of the organ remained. . . . On section the organs presented an intensely black colour, and the serum which flowed from the cut surface was of an inky hue. . . . When squeezed a fluid like ink could be expressed, which left a dark stain upon the hands. Repeated washing of a portion of lung diminished considerably the intensity of the colouration. On the surface of a portion thus treated different shades of pigmentation can be seen. Round or linear patches, ranging in size from a pea to a hazelnut, of an intensely black colour exist in large dark, slate grey areas. In many of these spots the air cells can still be detected, in others they appear to be obliterated, and the section in this case is uniform, not porous."[3]

Microscopical study of the dark fluid so readily expressed revealed that the color was due to black granules, some within cells, others free. Osler then proceeds to give a vivid description of phagocytosis. Among the cellular elements found in the expressed fluid are

> . . . corpuscles in which the bulk of the carbon is contained, and upon whose presence the black colour of the expressed juice in most instances depends. These are very variable in size, and may, on the one hand, approach the colourless blood corpuscles, and on the other, attain to five or six times their diameter. . . . In shape they are usually round, sometimes oval, occasionally irregular, very rarely approaching the spindle form. Inside all of these the carbon particles exist in extraordinary numbers, filling the cells in different degrees. Some are so densely crowded that not a trace of cell substance can be detected, more commonly a rim of protoplasm remains free, or at a spot near the circumference, the nucleus, which in these cells is almost always eccentric, is seen uncovered. The contained carbon particles are, for the most part, angular, and when not too thickly massed together, a reddish brown colour can be observed in each. In a few of them comparatively coarse portions of coal are found imbedded, stretching the cells to their utmost limits. . . . One curious specimen was observed: on an elongated piece of carbon three cells were attached, one at either end, and a third in the middle; so that the whole had a striking resemblance to a dumbbell. I could hardly

[2] Osler, William. On the pathology of miner's lung. *Canada med. surg. J.*, 1875–1876, *4*, 145–168.

[3] *Ibid.*, pp. 145–146.

credit this at first, until, by touching the top-cover with a needle and causing the whole to roll over, I quite satisfied myself that the ends of the rod were completely imbedded in the corpuscles, and the middle portion entirely surrounded by another. So strong was the attachment that I failed to separate any of the corpuscles by pressure on the top-cover and other manipulations. Another corpuscle was seen entirely surrounding the end of a small rod, forming a miniature drum-stick, the handle of which was twice as long as the diameter of the corpuscle.[4]

Osler goes on to point out that the pigment is to be found throughout the lung tissue, in the walls of the alveoli, at the point of junction of the fibrous septa, and in the interlobular connective tissue.

In addition to this case Osler also presented "several other specimens illustrating different degrees of pigmentation in the lungs." One of these, "comprising the lower lobe of one lung, was obtained from a Cornish miner who died under Dr. Howard's[5] care some years ago in the General Hospital of Pneumonia." Here, in addition to the intense blue-black color and the accumulation of carbon particles, Osler called attention to firm, indurated areas "composed entirely of fibrous and elastic elements, in the interstices of which the carbon granules" were densely arranged. Accompanying these indurated sections were dark emphysematous localities. In both cases the bronchial glands were hard and fibrous, and contained numerous carbon granules.

The third and fourth cases presented by Osler were not examples of "miner's lung," but he used them to illustrate several points in connection with the subject, as well as to aid in understanding the pathology of lung pigmentation. In his discussion of the specimens presented, Osler shows himself abreast of contemporary knowledge in this field. Of particular interest is his awareness that anthracosis and tuberculosis are distinct pathological conditions, and that the latter appears in the later stages of anthracosis, not at the outset.

From the description of the two first cases [Osler says] it is evident that we have here to deal with the early stage of the disease known as Miner's Lung, or, to give it the scientific appellation, Anthracosis. I say the early stage, meaning that the degenerative process can hardly be said to have commenced, and had not these men died of intercurrent affections, they might have lived for years under favorable hygienic conditions. No doubt, however, the point had been reached where further exposure to the impure air of the mines could only have resulted in bringing about serious lung trouble. Ultimately, as the records of *post mortems* show, there arise extensive areas of consolidation—carbonaceous Pneumonia, as it is called,—with numerous cavities containing an inky coloured fluid, and at last death takes place with many of the symptoms of chronic Phthisis, a peculiarity in some cases being the expectoration of a dark colored mucus. In the cases under consideration the intensely black consolidated spots

[4] *Ibid.*, pp. 149–150.

[5] Dr. Palmer Howard, Osler's teacher.

may be regarded as the first step in a series of degenerative changes. Such general infiltration of the tissues by a foreign matter cannot be without a strongly irritating action, the final effect of which would be a proliferation of the epithelial and connective tissue elements, with the result of obliterating the air cells and the formation of firm indurated areas. The larger these become, the more the cellular elements participate in the process, so much the more likely will they be to soften at the centres, and finally form cavities. . . . In the lungs of all individuals who die of this disease these cavities, which are no doubt often bronchiectatic, are described, surrounded by indurated areas, while the comparatively healthy sections are intensely black and emphysematous. . . . In some instances the continual inhalation of the dust in mines would appear to produce very little effect, for cases are mentioned of miners exposed for years to the same influences to which others succumb, and yet who were but slightly affected. Predisposition to lung disease is an important factor here, and it has been found that where this exists, they die at a much earlier age than those without this hereditary weakness, which need not, however, necessarily be a true tubercular diathesis. Indeed, in reading over the records of the *post mortems* in this disease, one is struck by the absence of any mention either of true tubercles or caseous masses, and in neither of the cases before us do these elements occur. . . . In its essence the whole disease would appear to consist in an overgrowth—a hyperplasia—of the fibrous tissue of the lungs, induced by the chronic irritation to which they are subjected by the inspired particles of coal dust, a veritable cirrhosis, or, as it might appropriately be called, the black Cirrhosis of miners. This certainly is the most natural view to be taken of these two cases, and accords best with their general and histological characters.

Finally, Osler concluded his discussion, "We are still in the dark as to how all this takes place, how the air cells become converted into firm hard areas . . ., or why, again, in the same lung, some of the intensely dark spots are solid, while others are emphysematous."[6]

Two other aspects of this report deserve attention. An unfailing passion for medical history and an indefatigable interest in research run through the career of William Osler, and both of these characteristics appear in the young professor's paper. Osler gives a succinct but very objective review of the controversy on the origin of pulmonary pigmentation. He reveals an acquaintance with the British, French, and German views on the subject, and correctly assigns the credit for advancing the knowledge of anthracosis.

Pointing out that the German and French students of lung pigmentation refused to recognize the external origin of anthracosis, he says:

The English observers (and with them several French), one and all, as far as my reading goes, from Pearson, who in 1813 first described the affection, took a more practical and common sense view, and attributed to it solely an extraneous origin. Having many more opportunities of observing the conditions under which miners worked and knowing the foul, sooty atmosphere of the mines, they were led to connect cause and effect, the dust with the disease, and so arrived at the truth years before

[6] Osler, *op. cit.*, pp. 158–160.

the Germans, to whom, however, the credit is due of having placed the fact upon an histological and experimental basis. They demonstrated the presence of dotted cells and other structures characteristic of vegetable tissue in the coarser particles obtained from the lungs, and, also, proved that the lungs of animals might be made of a dark color by exposing them for a length of time to a sooty atmosphere.[7]

Osler then demonstrated two particles of coal obtained from his cases.

Worth noting, however, is Osler's apparent ignorance of a brief report in 1869 by J. T. Carpenter, a Pennsylvania physician.[8] The fact that this account was published in the *Transactions of the Medical Society of the State of Pennsylvania* may explain why Osler was not aware of it. At any rate, Carpenter's statements are of considerable interest. "The penetration of solid, carbonaceous matter into the lungs," he claimed, "we all have verified by *post-mortem* examinations, as well as by the characteristic black sputa which accompany every case of bronchial or lung disease among miners."[9] Commenting on "miner's asthma," Carpenter pointed out that the condition "is chronic bronchitis, with thickening of the air-passages, emphysema and nervous distress in breathing. These chronic troubles may last a lifetime, without being rapidly fatal, or necessarily so. But acute pneumonia supervenes in many cases on some exposure and is very apt to prove fatal. If not, a chronic softening of the lungs may occur, in other words, phthisis, which is a frequent disease among these men and generally an incurable one."[10]

The last subject that Osler considers is the pathogenesis of anthracosis. After a preliminary reference to so-called physiological anthracosis, he explains that after passing through the alveolar wall, particles follow the course of the lymphatics. ". . . Where these are most abundant," Osler continues, "there the pigment is in the greatest quantity, as about the connective tissue of the vessels and bronchi, the interlobular septa, and, above all, just beneath the pleura. Once inside the lymphatic vessels a large proportion of the granules is carried on to the glands at the root of the lung, and is there permanently fixed in the cellular elements, hence the intensely dark colour of these in most persons over fifty. This fixation of the carbon granules in cellular bodies is very remarkable, and must be regarded as an effort of the economy to render harmless what might otherwise be very irritating substances."[11]

With reference to this phenomenon Osler reports experiments undertaken "to show the remarkable aptitude of cells to take up granules of vari-

[7] *Ibid.*, p. 161.

[8] Carpenter, J. T. Mining considered with regard to its effects upon health and life. *Trans. med. Soc. Penn.*, 1869, 5th ser., 2, 487–491.

[9] *Ibid.*, p. 489.

[10] *Ibid.*, p. 490.

[11] Osler, *op. cit.*, p. 163.

ous sorts, and, also to demonstrate the rapidity with which the lymphatic glands are affected. . . ."[12] In these experiments he injected the lymphatics of kittens with solutions of India ink to determine the distribution to the pigment particles. The experiments showed that irritating materials were taken up with great rapidity by the cellular elements. He describes phagocytic phenomena which impressed him greatly.

The conclusions with which Osler summed up his presentation were:

> 1. That in the early stage the process [in miner's lung] is confined to an increase in the fibrous elements about the bronchioles and vessels, and in certain emphysematous areas—a genuine Cirrhosis, or, as some would prefer to call it, an interstitial Pneumonia.
>
> 2. A considerable proportion of the carbon is contained in large cellular elements, which are specially abundant in the less pigmented, healthy portions, and in these it probably remains without much injury to the lung parenchyma. Another large part of the pigment lies free among the elements of the tissues, this being specially the case in the indurated spots, in the thickened pleura, and at the junction of the alveolar septa.
>
> 3. The extraneous origin of the carbon is proved by the detection in the lung of portions of fossilized vegetable tissue in the form of scalariform and dotted ducts.[13]

While at Montreal, Osler observed a number of other cases of miner's lung or miner's phthisis. In 1879, he published the case of a sixty-year-old metal miner.[14] As he remarks in his conclusion, this case supplements the one reported in 1875, where the disease was in an early stage. The pulmonary findings of extensive fibrosis and emphysema sustained his earlier conclusion that the essence of the disease appears to be a hyperplasia of the fibrous tissue of the lungs arising from chronic irritation.

On May 2, 1879 Osler presented a specimen of miner's lung to the Medico-Chirurgical Society of Montreal.[15] The following year, at a meeting of the Society on June 11, 1880, he presented another miner's lung.[16] According to the report of the meeting, this was the third case Osler had encountered in the autopsy room of the Montreal General Hospital in the previous three years.

No further case reports were forthcoming, but on May 10, 1881 Osler gave a lecture on a case of fibroid phthisis.[17] In the course of this lecture, he discussed fibroid phthisis due to the inhalation of dust, pointing out that this disease went under a variety of names—miners' phthisis, stone-cutters'

[12] *Ibid.*, p. 164.

[13] *Ibid.*, p. 168.

[14] Miners' phthisis. Reported by Mr. Rankine Dawson. Medical cases under Dr. Osler, *Canada med. surg. J.*, 1878–79, *7*, 452–454.

[15] I. Miner's lung; II. Atrophy of kidney. (Specimens presented, Medico-Chirurgical Society of Montreal, May 2, 1879.) *Canada med. Record*, 1878–79, *7*, 220.

[16] Medico-Chirurgical Society of Montreal, *Canada med. surg. J.*, 1880–81, *9*, 32.

[17] Osler, William. Clinical lecture on a case of fibroid phthisis. *Canada med. surg. J.*, 1880–81, *9*, 641–650.

phthisis, axe grinders' and file sharpeners' phthisis. "In the past five years," he said, "I have had three instances of this variety (that is, fibroid phthisis due to dust inhalation) under my care. I show you here a lung presenting what is known as the carbonaceous cirrhosis, or miners' phthisis. You see that the greater portion of it is converted into a mass of firm, dark tissue, looking more like a bit of hard coal than a lung. The greater portion is indurated by this growth of fibroid tissue and the deposition of these dark carbonaceous particles. That the dark coloring matter in the lungs is due to the inhalation of coal particles, is proved by the fact that on examination you can see portions of the vegetable tissue of the coal."[18]

It is interesting to note that while Osler employs the terms *anthracosis* for coal miner's phthisis and *siderosis* for the form of fibroid phthisis to which workers in iron mines are subject, he does not use the term *pneumonoconiosis* recommended by Zenker in 1867 to designate all pulmonary conditions resulting from the inhalation of dust. This is all the more noteworthy as it was Zenker who proposed the term siderosis.

With Osler's departure from Montreal his contributions on miner's lung cease. However, his interest in the subject did not end, for in 1889 he refers to it in a broader context. On April 3, 1889 he addressed the Alumni Association of Bellevue Hospital in New York, the subject of his address being "On Phagocytes."[19] In connection with phagocytosis as a physiological process and its significance in pathological conditions, he called attention to "the remarkable activity of the pulmonary phagocytes."[20]

Discussing dust inhalation and the rôle of the cellular elements in disposing of inhaled particulate matter, Osler remarked that to see the steps in this process in perfection ". . . one must study the early stages of anthracosis, particularly in those exceptional cases which we see occasionally when a miner has been killed by accident or dies of acute disease."[21] He then describes the phagocytic phenomena that had been observed in the case which he had reported in 1875. In this discussion Osler also refers to the extensive study of experimental pneumonoconiosis published by Arnold in 1885, thus indicating again his interest in the subject and his knowledge of the relevant literature.

William Osler's contribution to the study of miner's lung may now be summed up. Most significant is his emphasis on the phagocytic process. The theory that the endothelium is the source of phagocytic cells, capable of wandering into the alveoli and removing any foreign particles present

[18] *Ibid.*, p. 647.

[19] Osler, William. On phagocytes. *Med. News*, 1889, *54*, 393–396, 421–424.

[20] *Ibid.*, p. 395.

[21] *Ibid.*, p. 395.

there, was suggested by Slavjansky in 1869 on the basis of his experiments.[22] In 1876 von Ins was able to show that dust in the alveoli is removed by phagocytic cells (leukocytes) and transported into the interstitial tissue in this manner.[23] Osler thus precedes von Ins and in some measure anticipates his work. His report of 1875 with its observations on the activities of phagocytic cellular elements in the lungs and with the results of his experiments on the distribution of pigments by the lymphatics clearly points in the direction whence advances in the knowledge of the subject were to come. In addition, he added further evidence to substantiate the external origin of pulmonary pigmentation in miners. Finally, in these papers on miner's lung can be seen those qualities which made Osler an outstanding teacher and doctor. The ability to fuse pathology, clinical medicine, history, and experimental research into an organic unity, and to view medical problems from a broad biological viewpoint, is clearly evident in these early studies.

[22] Slavjansky, K. Experimentelle Beiträge zur Pneumonokoniosis Lehre. *Virchows Arch.*, 1869, *48*, 326–332.

[23] Ins, A. von. Experimentelle Untersuchungen über Kieselstaubinhalation, *Arch. exp. Path. Pharmak.*, 1876, *5*, 169–194.

Chiron the Centaur

WARREN R. DAWSON*

"If the poet's tongue might voice the prayer that is on the lips of all, I would pray that Chiron, the son of Philyra, who is dead and gone, were now alive again."
—PINDAR

CHIRON the Centaur, the tutor of Asclepius (or Æsculapius), is a prominent figure in the legendary history of medicine and a personality who had in early times won a high reputation. Classical literature is full of allusions to his wisdom and prestige. The reputation of Chiron survived until the Middle Ages, and his name is still associated with more than one medicinal herb.

The Centaur Chiron was the offspring of Cronus (Saturn) and Philyra, a daughter of Ocean. She was a sylvan nymph, associated with the lime-tree.[1] Cronus met with her in Thessaly, and, according to some accounts, transformed himself into a horse in order to escape the notice of his wife Rhea; according to others, he assumed equine shape because Philyra had turned herself into a mare in order to elude him.[2] On the birth of their child, Philyra was so distressed when she beheld it that she prayed to be transformed into some other shape. Zeus answered her prayer, and she became the lime tree.[3] Apollonius Rhodius says: "She brought forth mighty Chiron, half like a horse, half like a god."[4] Other writers speak of Chiron as "a Centaur of double form,"[5] or as "a half-man, compounded of the body of a tawny horse,"[6] and Lucan says only that he had the feet of a horse.[7]

The Centaurs, of which there were many, were a wild, uncouth and lawless race. Most of them were the offspring of Centaurus (Kentauros), the son of Ixion and Nephele, their mothers being high-spirited Magnesian mares.[8] They dwelt in caves about Mount Pelion in Thessaly, living free, drunken and sensuous lives. Chiron dwelt amongst them, but his charac-

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[1] Her name and that of the lime or linden tree (φιλύρα) are identical. For the peculiarities of the linden, see Theophrastus, *Hist. Plant.* i, 12, 4, and for its use in divination, Herodotus iv, 67.

[2] Apollonius Rhodius, *Argonautica,* ii, 1231–1241, says that Cronus was surprised by Rhea and became a horse in order to escape her. See also the Scholiast on that passage; Apollodorus i, 2, 4; Virgil, *Georgics,* iii, 91–93; Ovid, *Metamorphoses,* vi, 126.

[3] Scholiast on *Argonautica,* ii, 1231.

[4] *Argonautica,* ii, 1240–1241.

[5] διφυὴς Κένταυρος. Apollodorus, i, 2. 4.

[6] Semivir et flavi corpore mixtus equi. Ovid *Fasti,* v, 380.

[7] *Pharsalia,* lxxv, 15.

[8] Diodorus Siculus, iv, 69; Apollodorus, *Epitome,* i, 20; Pindar, *Pythian Odes,* ii, 44–48.

ter and pursuits differed wholly from theirs. He was just, gentle, righteous and learned, and friendly both to gods and men. He was highly skilled in the arts of hunting, music and medicine, and in popular tradition was held to be the discoverer of the medicinal values of simples and of the methods of using them. His amiable disposition is evidenced in many ways, and in this connection reference may be made to the greeting he gave to the Argonauts as their ship sped from the shores of Thessaly. "And down from the mountain-top to the sea came Chiron Philyrides,[9] and where the foaming surf broke he dipped his feet, and with much waving of his massy hand, he wished them a happy home-coming and a safe voyage."[10] Homer speaks of Chiron as "the most just of Centaurs"[11] and his wise and kindly character is often referred to by others.[12] His praises have been very beautifully sung by Pindar: "If the poet's tongue might breathe the prayer that is on the lips of all, I would pray that Chiron, son of Philyra, who is dead and gone, were now alive again,—he who once ruled far and wide as the offspring of Cronus, who was the son of Heaven. Would that that rugged monster with spirit kindly unto men were reigning still in Pelion's glens, even such as when, in olden days, he reared Asclepius, that gentle craftsman who drove pain from the limbs that he healed,—that hero who gave aid in all manner of maladies."[13]

Chiron's gentleness, wisdom and strength made him eminently fit to be the protector and instructor of children and many of the most celebrated heroes of Greece were brought up and taught by him. The list of Chiron's pupils is a long one, but first and foremost comes Asclepius, himself destined to become the god of medicine. Reference has already been made, in the passage just quoted from Pindar, to Chiron's tutorship of Asclepius. Apollodorus relates that the infant Asclepius, the child of Apollo and the nymph Coronis, was snatched by Apollo from his mother's arms as she was burning on the pyre (for such was her punishment inflicted by her divine spouse for playing him false), and taken by him to Chiron, by whom the child was reared and instructed in the arts of healing and hunting. Asclepius gained great fame as a surgeon and he brought his craft to such a pitch that he could not only avert disease and heal the sick, but could even raise the dead.[14] Apollodorus goes on to state the names of some of

[9] That is to say, Chiron the son of Philyra. This name is often bestowed upon him: e.g., Hesiod, *Theogony*, 1002; Pindar, *Pyth. Odes*, iii, i; ix, 30; Ovid, *Ars Amatoria*, i, 11; *Fasti*, v, 391; etc.

[10] Apollonius Rhodius, *Argonautica*, i, 553–6.

[11] *Iliad*, xi, 832.

[12] E.g., Hyginus, *Astronomica*, ii, 38; Virgil, *Georgics*, iii, 550; Ælian, *De Nat. Animalium*, ii, 18; Euripides, *Iphigenia in Aulis*, 705–710; etc.

[13] Pindar, *Pyth. Odes*, iii, 1–7. The translation here quoted is that of Sir John Sandys.

[14] Apollodorus, iii, 10, 3. Other accounts in Pindar, *Pyth. Odes*, iii, 24–67; Pausanias, ii, 26, 6; Ovid, *Metamorph.* ii, 590–632.

those whom, being dead, Asclepius restored to life, and supplies the interesting detail that he was enabled to raise the dead by means of the blood of the Gorgon, given to him by Athena. He used the blood that had flowed from the veins on the left side of the monster's body as a poison for mankind, and blood from the right side for their salvation (πρὸς σωτηρίαν).[15] Pindar again says of Asclepius: "And those whosoever came suffering from the sores of nature, or with their limbs wounded, either by gray bronze or far-hurled stone, or with bodies wasting away with summer's heat or winter's cold, he loosed and delivered divers of them from diverse pains, tending some of them with kindly incantations, giving to others a soothing potion, or, haply, swathing their limbs with simples, or restoring others by the knife."[16] Apollodorus relates that the skill and success of Asclepius were such that Zeus grew jealous of his powers and killed him with a thunderbolt.[17] Diodorus Siculus gives a different version: he says that the success of Asclepius in healing the living and raising the dead had so reduced the population of the underworld that Zeus slew him because of the complaints of Pluto that his domain was becoming impoverished.[18] Pindar ascribes yet another motive for the vengeance of Zeus. "But, alas!" he said, "even the lore of leech-craft is enthralled by the love of gain; even he [Asclepius] was seduced by a splendid fee of gold displayed upon his palm, to bring back from death one who was already its lawful prey. Therefore the son of Cronus with his hands hurled his shaft through both of them and quickly reft the breath from out their breasts for they were stricken with sudden doom by the gleaming thunderbolt."[19]

According to a late tradition, Apollo himself, the father of Asclepius, had been taught by Chiron.[20]

Another son of Apollo, the rustic deity Aristaeus, whose mother was Cyrene, was also trained by Chiron. Cyrene bore the infant on Mount Pelion, and the babe was carried to the cave of Chiron, there to be reared. Chiron taught Aristaeus the arts of healing and of prophecy.[21] Chiron himself had prophesied that on the birth of Aristaeus, the nymphs would drop nectar and ambrosia upon his lips and that he should be a guardian of flocks.[22] Aristaeus grew up and was wedded to Autonoë, the daughter of

[15] Apollodorus, *loc. cit.*; cf. Euripides, *Ion*, 999. Amongst those restored to life by Asclepius were Capaneus, Lycurgus, Hippolytus, Tyndareus, Hymeneus, and Glaucus, son of Minos.

[16] Pindar, *Pyth. Odes*, iii, 82–93 (Sir John Sandys' translation). It will be observed that the methods of Asclepius, like those of other primitive physicians, were partly magical, partly therapeutic, and partly surgical.

[17] Apollodorus, iii, 10, 3.

[18] Diodorus, iv, 71.

[19] Pindar, *Pyth. Odes*, iii, 54–8. (Sandys.)

[20] Justin Martyr, *De Monarchia Dei*, vi.

[21] Apollonius Rhodius, *Argonaut*, ii, 508–512. According to Diodorus Siculus, iv, 81, Aristaeus was reared by the nymphs.

[22] Pindar, *Pyth. Odes*, ix, 59–65; cf. *ibid.*, 29–64.

Cadmus,[23] and their child was Acteon the hunter. Acteon, like his father, was placed in the Centaur's care, and Chiron taught him his craft; but he came to a terrible end, for he was devoured by his own dogs. According to Apollodorus, Acteon met his death through the vengeance of Artemis, whom he had seen bathing with her attendant nymphs. The goddess transformed him into a deer and incited his pack of hounds to give chase and to kill and devour the animal. When they had done this, they sought their master, and whining pitifully, came to the cave of Chiron, who fashioned an image of Acteon to console the grief of the faithful dogs who had, all unknowingly, destroyed their master.[24]

Chiron reared Achilles, of all Greek heroes the most renowned, the son of Peleus and Thetis. Peleus brought his infant son to the cave of Chiron who received the child and fed him upon the entrails of lions and wild-boars and upon the marrow of bears.[25] This diet was evidently intended to impart to the child the strength and courage of the wild beasts. But according to Philostratus, the diet of the infant was of a gentler kind, and consisted of honeycombs and the marrow of deer, whereby he would become, on the same principle, sweet of disposition and fleet of foot.[26] Chiron instructed Achilles in the art of healing with simples[27] and also taught him to perform upon the lyre.[28] According to tradition there was a book of the Precepts of Chiron for the instruction of Achilles.[29] When Chiron greeted the departing Argonauts, the infant Achilles was brought out in order that his father might see him.[30]

Jason, too, was reared by Chiron, and he spoke of his tutor as "the divine Centaur."[31] Medeus, Jason's son, was also received by Chiron,[32] as was Melampus, who became a skilled magician and knew the language of the birds.[33] Tradition ascribed other gods and cult-heroes to the care or influence of Chiron. Amongst these are Dionysus,[34] Podalirius and Machaon, the sons of Asclepius,[35] and Phoenix, the son of Amyntor. Phoenix had been

[23] Apollodorus, iii, 4, 2.

[24] Apollodorus, iii, 4, 4; Diodorus Siculus, iv, 81 (who omits the mention of Chiron and the image); Ovid, *Metamorph.* iii, 131–252, tells the story with much poetic detail.

[25] Apollodorus, iii, 13, 6.

[26] Philostratus, *Heroica,* xx, 2. For many instances of the eating of parts of wild animals in order to acquire their attributes, see Sir J. G. Frazer, *The Golden Bough,* ed. 3, *Spirits of the Corn and of the Wild,* vol. ii, ch. xii, pp. 138 *seqq.*

[27] Homer, *Iliad,* xi, 830–832.

[28] Ovid, *Ars Amatoria,* i, 11–16.

[29] Χείρωνος Ὑποθῆκαι. This was attributed to Hesiod; see Pausanias, ix, 31, 5. For other references to Chiron's tutorship of Achilles, see Pausanias, iii, 18, 2; Plutarch, *De Vita Homeri,* ccii; Lucan, *Pharsalia,* x, 15, 1; Ælian, *De Nat. Anim.* ii, 18; Pliny, *Nat. Hist.,* xxv, 19.

[30] Apollonius Rhodius, *Argonaut.,* i, 558.

[31] Pindar, *Pythian Odes,* iv, 101–119; *Nemean Odes,* iii, 54. For the word φήρ, applied to the Centaurs, cf. Homer, *Iliad,* i, 268; ii, 743.

[32] Hesoid, *Theogony,* 1000–2.

[33] Columella, *De Re Rustica,* x, 349; Virgil, *Georgics,* iii, 558, Apollodorus, i, 9, 11.

[34] Ptolemaeus Hephaestionis, *Nova Historia,* iv.

[35] Xenophon, *Cynegeticus,* i, 2.

blinded by his father on a false charge of having seduced one of his concubines. Peleus brought him to Chiron who restored his sight, and he then became king of the Dolopians.[36]

Chiron rescued Peleus from the plot against his life engineered by Astydamia, the wife of Acastus, when he rejected her guilty overtures. She falsely accused Peleus to her husband of having attempted her virtue.[37] Acastus, who was engaged in a contest with Peleus, accordingly deserted him, and whilst Peleus was sleeping on the slopes of Mount Pelion, Acastus took from him his sword and hid it in cows' dung. Peleus, awaking, sought in vain for his weapon and, thus disarmed, was caught by the Centaurs who would have destroyed him but for the timely aid of Chiron who rescued him and recovered and restored his sword.[38] Chiron was ever friendly to Peleus: on his marriage with Thetis, Chiron gave to Peleus a magic spear of ash-wood,[39] and, as already noted, he took charge of Peleus's infant son Achilles.

Chiron did not live alone: he had a wife and daughters who shared with him the responsibilities of rearing the various children that were placed in his charge. When Chiron came to the water's edge to bid farewell to the departing Argonauts, he was accompanied by his consort (παράκοιτις) who carried the infant Achilles in her arms and showed the child to his father.[40] She is not named by Apollonius Rhodius, but we know from Ovid that Chiron had a daughter by Chariclo,[41] presumably the same Chariclo, a nymph, who became by Everes (the son of Udaeus, one of the Spartans who sprang from the dragon's teeth of Cadmus) the mother of Tiresias, the blind seer.[42] Pindar speaks of Chariclo in conjunction with Chiron and his mother Philyra, but he does not say that she was his wife, and in the same passage he mentions "the pure daughters of the Centaur,"[43] of whom not one is named. According to Ovid, the name of Chiron's daughter by Chariclo was Ocyrrhoë. The girl was skilled in her father's arts and was also endowed with the power of prophecy. She predicted that Asclepius would become so skilled as a physician that he would incur divine wrath, would perish by a thunderbolt, but would live again as a god. Of her father Chiron,

[36] Apollodorus, iii, 13, 8; Propertius, ii, 1, 60. Homer, *Iliad*, ix, 437–484, gives a different version of the accusation against Phoenix, and does not mention his blindness nor Chiron's cure.

[37] The false accusation by the guilty wife is frequent in folk-lore and mythology. It occurs in the ancient Egyptian "Story of the two brothers" and in the well-known episode of Potiphar's wife. Many instances have been collected by G. Maspero, *Popular stories of Ancient Egypt*, London, 1915, Introduction, pp. xvii–xx.

[38] Apollodorus, iii, 13, 3; Pindar, *Nemean Odes*, iv, 92–100 (who calls Acastus's wife Hippolyta).

[39] *Iliad*, xvi, 140; Apollodorus, iii, 13, 5.

[40] Apollonius Rhodius, *Argonaut.* i, 557–8.

[41] Ovid, *Metamorph.* ii, 636.

[42] Apollodorus, iii, 6, 7.

[43] Pindar, *Pyth. Odes*, iv, 102–3.

she predicted that he, though born immortal, would long to die on being tormented by the poisonous blood of a dire serpent, and that his wish would be granted. Like many other prophetesses who foretold the future, the utterances of Ocyrrhoë brought upon her head the wrath of the gods: her voice failed and she could utter words no more, her face and her limbs changed their form, her fingers and toes coalesced into hoofs, and she became a mare, neighing and cropping grass, her flowing locks transformed into a mane.[44]

The death of Chiron is one of the most picturesque episodes in Greek mythology: it came about in this wise. Hercules, in search of the Erymantian boar, came to Mount Pholoe in Arcadia, and was there entertained by the Centaur Pholus[45] in his cave. After eating his victuals Hercules called for wine, of which Pholus had but a single jar, and this he feared to open because it was not his own property but belonged to all the Centaurs in common.[46] Yielding at length to the entreaties of his guest, Pholus broached the jar and the scent of the wine at once attracted all the other Centaurs who rushed to the cave armed with stones and tree-trunks. Two of them, bolder than the rest, entered the cave but Hercules repelled them with brands. Of the rest, some were killed, and others were pursued to Malea, where Chiron had taken up his abode after the Centaurs had been expelled by the Lapiths from Mount Pelion.[47] Here the fugitives took shelter in Chiron's cave, and Hercules shot an arrow at them. By accident the weapon struck Chiron upon the knee, and Hercules, deeply distressed, rushed to the assistance of the wounded Centaur, drew out the arrow and applied a healing herb. All was of no avail, for the wound was mortal; but Chiron, being immortal, could not die, though he longed for death. Prometheus offered himself to Zeus to be immortal in Chiron's stead, and Chiron, thus released from immortality, died. Thereupon the Centaurs scattered and fled in all directions, save only Pholus who returned to his cave. Pholus took up an arrow that had killed one of his fellows and as he examined it, it slipped from his hand, pierced his foot, and instantly killed him. Hercules then buried Pholus and departed to continue his quest for the boar.[48]

[44] Ovid, *Metamorph.* ii, 632–675.

[45] Pholus was the son of Silenus and a tree-nymph (Ash). He, like Chiron, was amiable and gentle and altogether different in his nature from the other Centaurs.

[46] Diodorus Siculus, iv, 12, states that this wine-jar was the gift of Dionysus who ordered that it should not be opened until Hercules should come.

[47] The fight with the Lapiths was caused by the attempt by the Centaurs to carry off Deidamia (called Hippodamia by Diodorus), on the day of her marriage with Pirithous, king of the Lapiths and son of Ixion. It ended in the expulsion of the Centaurs, who were driven from Pelion with the help of Theseus. See Diodorus Siculus, iv, 69, 70; Plutarch, *Theseus,* 30; Ovid, *Metamorph.* xii, 210–535.

[48] Apollodorus, ii, 5, 4.

Such is the outline of the story as related by Apollodorus. It is retold elsewhere, but with many variations of detail. Diodorus Siculus gives an account which is in the main the same as that of Apollodorus, but it is more detailed in its description of the combat between Hercules and the Centaurs.[49] Ovid presents a widely different version which omits all reference to Pholus and the other Centaurs and asserts that Chiron himself, fingering the shafts in the quiver of Hercules, dropped one of them upon his left foot and so compassed his own death.[50] According to others, it was not Chiron, but a Centaur named Pylenor, who was killed by the arrow of Hercules.[51]

Thus was the prophecy of Chiron's daughter fulfilled. She had declared that her father, though immortal, would long for death,[52] and that his death would be caused by the blood of a dread serpent. The arrows of Hercules were poisoned, according to Ovid with the blood,[53] and according to others with the gall,[54] of the Hydra.

When Chiron exchanged his immortality with Prometheus, he became the constellation Sagittarius, or the Centaur.[55] But the kindly Centaur, thus elevated to the skies, still had his cult upon earth, for the Magnesians sacrificed to him as a divine physician, and offered to him the first-fruits of their herbs.[56]

Many plants are associated with Chiron's name. The four panacæas—Asclepion, Heracleon, Chironion and Centaurion—were said to have been discovered by him.[57] Chiron was also the discoverer of the white Bryony, the *Ampelos chironia* of Pliny and the *Bryonia alba,* L., of botanists.[58] The Centaurea is said to have healed Chiron when the arrow of Hercules pierced his foot, but according to the accounts of his death quoted above, the wound was mortal and could not be healed. His name was also given to open ulcers that refuse to heal: "Old ulcers which are difficult to cicatrize are called Chironian, as if requiring Chiron himself to heal them."[59]

The name of Chiron the Centaur has become intimately associated with the *Herbarius* of Apuleius. This herbal was very popular in the Dark Ages, and many manuscripts of it are known. The author of it is alleged

[49] Diodorus Siculus, iv. 12.
[50] Ovid, *Fasti,* v, 391–408.
[51] Pausanias, v, 5, 10.
[52] Lucan, *Pharsalia,* x, 26.
[53] Ovid, *Metamorph.* ii, 652; *Fasti,* v, 403.
[54] Diodorus Siculus, iv, 11; Pausanias, ii, 37, 4.
[55] Ovid calls the constellation *Chiron,* and asserts that it is composed of fourteen stars (*Fasti,* v, 413). Ptolemy gives the number of stars as thirty-seven. The constellation is mentioned by Eudoxus (4th cent., B.C.) and by Aratus (3rd cent., B.C.).
[56] Plutarch, *Quæstiones Conviviales,* iii, 1, 3.
[57] Pliny, *Nat. Hist.* xxv, 11–14. These four plants have been identified respectively with *Echinophora tenuiflora,* L.; *Laserpitum chironium,* L.; *Hypericum olympicum,* L.; and *Centaurea centaurium,* L.
[58] Pliny, *Nat. Hist.* xxv, 16; xxiii, 17.
[59] Paulus Ægineta, iv, 46.

to be Apuleius Platonicus Madaurensis, but sometimes he is called Apuleius Barbarus or Pseudo-Apuleius. The latter designations are modern and serve to distinguish the author of the herbal from that of Lucius Apuleius, the Platonic philosopher and rhetorician who was born in Numidia in the year 125 A.D. But by whatever name he may be called, the actual author or compiler of the *Herbarius* is unknown to us; there is internal evidence that the work is a translation or adaptation of a Greek prototype, but no Greek manuscript of it is known, unless, as seems probable, the fragmentary *Johnson Papyrus,* a single folio from a papyrus codex written about 400 A.D., is the sole surviving relic of a Greek original.[60] The latest critical edition of the Latin text is that of Howald and Sigerist, published in 1927.[61] The Latin version of the *Herbarius* was probably compiled in the fourth century A.D., but no manuscript of it is known of earlier date than the seventh. It was translated into Anglo-Saxon in the twelfth century[62] and it long retained its popularity in northern Europe. Most of the extant manuscripts ascribe the book to Chiron the Centaur and those that are illuminated have a picture of him. The title reads as follows:

> Herbarius Apulei Platonici quem accepit a Chirone Centauro, magistro Achillis, et ab Aesculapio.[63]

In the Anglo-Saxon manuscript in the British Museum the volume opens with a large and beautifully illuminated picture in which, according to some interpreters, Plato hands the book to Asclepius and Chiron. The central figure, in Saxon costume, holds the volume, bound in red leather: on his right is Asclepius, a bearded man in Greek costume, and on his left stands Chiron in his traditional guise—*i.e.,* a bearded man with human head, arms and torso attached to the body and legs of a bay horse. The three figures have their names written below them: the central figure is labelled Plato, and the other two Escolapivs and Centavrvs respectively. It seems to me more probable that in writing "Plato" beneath the central figure, the scribe was deceived by the title of the book—"Herbarium Apulei Platonici." The title states quite specifically that Apuleius received the book from Asclepius and Chiron, and it seems more probable that the picture is

[60] This papyrus was discovered at Antinoe in Egypt in 1904 by Dr. J. de M. Johnson, who was then excavating for the Egypt Exploration Fund, and it is now in the Wellcome Museum in London. The Johnson Papyrus and its relation to the extant manuscripts of the *Herbarius* have been interestingly discussed by Dr. Charles Singer in the *J. Hellenic Studies,* 1927, *47,* 31, 43, and it is reproduced in colour in the same publication, pl. i and ii.

[61] *Corpus Medicorum Latinorum,* vol. iv, Leipsic, 1927.

[62] The best known codex is Cotton, Vitellus, C. iii, in the British Museum, edited by O. Cockayne in *Leechdoms, Wortcunning and Starcraft of Early England,* vol. i, London, 1864.

[63] For the variants, see Howald and Sigerist, *op. cit.,* p. 15.

intended to represent Apuleius receiving the book than Plato bestowing it. Other manuscripts present variants of this picture.

Especially associated with Chiron is a particular herb, three kinds of which are described in Chapters X, XI and XII of the *Herbarius*. This is the Artemisia, a plant well known by its vernacular name Mugwort. Of these three kinds it is said:

> Nam has tres artemisias Diana dicitur invenisse et virtutes earum et medicamina Cironi centauro tradidit, qui primum de his herbis medicinam instituit. Has autem herbas ex nomine Dianae, hoc est artemisiam nuncupavit.[64]

In many of the manuscripts there is a picture of Chiron receiving the plant from Artemis (Diana). The herb has enjoyed a reputation from very early times and has an elaborate story of its own, which cannot be dealt with here.

Finally it may be mentioned that the name of Chiron has an association with veterinary medicine. Suidas[65] says that a book on the veterinary art was composed by Chiron, and tradition accordingly associated his name with a later work of the Middle Ages known as the *Mulomedicina Chironis* of which several manuscripts are known.[66]

[64] *Herbarius*, xii, 2.

[65] *Lexicon*, s.v. Χειρων.

[66] Edited by E. Oder, *Claudii Hermeri Mulomedicina Chironis*, Leipsic, 1901. See also F. Bullock, *Proc. Third Internat. Congress Hist. Med. London, 1922* (published in Antwerp, 1923), pp. 304–05, and *J. comp. Path.*, 1922, *35*, 305–309.

"The Bewitchment of the Infinitely Small"

Spain's Greatest Scientist Begins a Lifetime of Research in the Minute Anatomy of the Nervous System*

DOROTHY F. CANNON†

BY the year 1884 when Santiago Ramón y Cajal, now thirty-two years old, transferred to his new position at Valencia he had won the reputation of being a hard-working, earnest investigator. Upon moving to Valencia in January, he and his family took temporary lodgings in a hotel on the Market Square near the old Silk Exchange, one of the last remaining examples of Spanish medieval civic architecture. When they had succeeded in finding a suitable house and in buying the new furniture they needed for it, they went to live in a simple dwelling in the Calle de las Avellanas, where a few days later a second daughter, Paula, was born. Cajal was now the father of three children. The two eldest were a girl and a boy, Fé and Santiago.

Cajal was charmed with Valencia and spent a few days before becoming immersed in his work in exploring the romantic old city. He visited the ancient cathedral and climbed its tower, the Miguelete. He filled his eyes with the deep green-blue of the Mediterranean. He made excursions to the picturesque suburbs and the enchanting little towns near by. He wandered about the seaport, the popular promenade, and the ruins of the Roman theater at Sagunto.

He soon made friends with his colleagues at the university and found them to be an excellent group of men. This is how one of them describes him in the early days in Valencia:

> In 1884 a young professor who had just won by competitive examination the chair of anatomy at the university, appeared among us. It was Cajal. His somewhat neglected person had a dry, angular, rugged look about it. If this made him seem a bit uncouth, it was at once redeemed by his noble head. His forehead was broad and was made still broader by incipient baldness, by the slight depressions at his temples, and his fine, straight nose. These gave him the stamp of intellect and distinction. His black eyes were remarkable too, their gaze dreamy when deep thought seemed to draw them back into his head, yet keen and penetrating when focused upon something in rapt attention. . . . In spite of his blunt frankness and his temperament, which was more inclined toward seriousness than laughter, he quickly adapted himself to the gay atmosphere of the city and he soon gained the respect of both faculty and students by his learning. He won my friendship at once and shortly gave me his.

* A chapter from the recently published biography of Cajal, *Explorer of the human brain*, New York, Henry Schuman, Inc., 1949.

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In order not to become too one-sided in his almost fanatical absorption in microscopy, Cajal joined a social club, the Casino de la Agricultura, where he moved in a circle of agreeable and distinguished people. He became an ardent chess player, his only "vice." He joined a scientific and literary society, too, and there met some of the outstanding intellectuals of Spain. These were his sole extravagances, and he felt they were justified in that they saved him from the gaucherie and mental lopsidedness that characterize so many scientists who devote their time and energies to specialization in such restricted fields as he now contemplated for himself.

His home was modest, for to him a balanced budget was a strict necessity. Without it, he realized, neither domestic peace is possible, nor that tranquillity of spirit so indispensable to prolonged research without expectation of monetary returns. His house had a large room well suited to become his new laboratory, and it was soon full of activity. A busy laboratory, he found out, is about as expensive as a rapidly growing family—and he now had both, so he was well qualified to judge. To supplement his professorial salary, he chose to do outside teaching rather than to resort to medical practice, which would leave him scant leisure for the research work now occupying the center of his thoughts. From the first he was very successful in his teaching, and he soon organized a course in normal and pathological histology. His lectures were attended by several physicians working for the doctorate and by others already in practice who wished to extend their knowledge, particularly in the new science of bacteriology, which was now rapidly winning a place for itself as a result of the brilliant work of Pasteur and Koch.

The additional income he earned in this way put his laboratory on a soundly functioning financial basis, and even enabled him to buy some new equipment that he badly needed, such as an automatic microtome. Because he was miserably poor, he used small animals, chiefly mice, for his experiments and would put a dozen different specimens on a slide. His choice of the mouse, one of the smallest mammals, made it possible for him to follow through all the structures of the brain in a relatively small number of sections. And because the nuclei of the cells were close together, he could see the nerve processes extending all the way to their destinations. In this manner he was able to observe the whole architecture of this mammal's brain more completely than it had ever been done before.

Though he was managing by extracurricular work and rigid economy to put his home laboratory on a fairly efficient basis, his facilities for teaching anatomy at the university remained meager. He pleaded with the Min-

ister of Education to make it financially possible for the university to get better equipment for its students, promising that if this were done, he would see to it that their original work in his department would win a place comparable with that held by the university laboratories of France and Germany. "It is a disgrace," he said, "that among the many thousands of discoveries there is not one to which the name of a Spaniard is attached."

A little help was given, and Cajal kept his promise. Within the next few years, a series of articles on various aspects of brain anatomy issuing from Valencia began to attract the attention of the medical world. The new discoveries hinted at in these early publications were so different from the views generally held with reference to the intimate construction of the brain substance that they were largely discredited. Perhaps remembering this experience and many like it that came to him in later years, Cajal would write in his *Charlas de Café* (*Conversations at the Café*) with a touch of bitterness: "To be right before the right time is heresy, sometimes to be paid for with martyrdom." The more vigorous champions of the old concepts questioned the accuracy of his observations; the more open-minded were still to be convinced. Yet in less than ten years Cajal's discoveries would become an essential part of all histological knowledge of the nervous system.

THE CHOLERA EPIDEMIC OF 1885

Cajal's scientific progress was suddenly interrupted in 1885 by the cholera epidemic that raged that year in Valencia and later throughout all Spain. Although Robert Koch had recently discovered the comma bacillus to be the cause of cholera, this knowledge had as yet been put to little use. Microbiology was then only in its birth throes but it was already stirring up widespread interest and enthusiasm. Many of the older histologists were deserting their earlier specialty to devote their energies to the virgin territory opened up by the study of pathogenic bacteria and the ways by which these microscopic organisms cause infection, illness, and death in men and animals. Cajal, too, was momentarily attracted to it.

For years afterward, the horror of the cholera epidemic remained vividly in his memory. The hospitals were bursting with victims; in Cajal's own street there were several cholera deaths, though fortunately his own family escaped unscathed. There was bitter controversy among the doctors: those loyal to the teachings of the old school held that the cause of the disease was the mist of the night air and administered laudanum, as advocated in the

seventeenth century by Sydenham; those of the new school, mostly younger men, recommended boiling the drinking water and taking no food that had not been thoroughly cooked. It was by following these simple precautions that Cajal's family preserved its immunity, in spite of the fact that his laboratory was full of cultures of cholera in gelatin and broths. When the epidemic was at its height, his fourth child, Jorge, was born, on July 2, 1885.

At just this moment the eminent Dr. Ferrán came to Valencia, preaching the new gospel of the anticholera vaccine. After several experiments on guinea pigs and several in which he had heroically inoculated himself, he was convinced that he had found a culture of the disease which, when injected into a man, would immunize him against the microbe if it should enter his body through his mouth. The medical profession heatedly debated the subject of the new vaccine and as usual was divided into two opposing camps of old and young, of conservatives and progressives. The older men declared the vaccine to be a gross scientific error, if not an out-and-out money-making quack remedy. But the devotees of Dr. Ferrán were not to be put aside. They organized a society for the purpose of spreading information about the use of the vaccine, of manufacturing it on a large scale, and of obtaining from the Government permission to immunize all the people living in the districts in which the epidemic was raging. Cajal was urged to become a member of the society. But he was not absolutely sure of the efficacy of the vaccine and wished to remain open-minded and free from any taint of mercenary motives, so he did not join it. Still, since he was a resident of Valencia and busy with work in microscopy, the provincial government of Zaragoza appointed him, together with Dr. Lite, the official delegate, to study both the disease itself and the proposed preventive measure and to prepare a statement on the subject.

Cajal threw himself into this task and in July, 1885, he traveled to Zaragoza to give his report. By this time the epidemic had spread throughout almost the whole of Spain. He confirmed the theory, then still disputed, that the disease really was cholera and stated that in all probability it was due to the comma bacillus of Koch. But he was not inclined to put much faith in the anticholera vaccine prepared by Dr. Ferrán. He felt that its effectiveness had not yet been proved and that further study was needed before such a potentially dangerous culture should be widely administered in vaccine form.

By the end of September, Cajal had completed work on a large monograph prepared at the request of the provincial government of Zaragoza—*Studies on the Red Microbe of Cholera and Prophylactic Inoculation.* In

spite of the fact that such a work would necessarily be chiefly a summary of information on the subject to date, with a careful evaluation and interpretation of the known facts, Cajal's report did contain some original conclusions based on his own experiments. One was a new, practical, and simple method for staining the comma bacillus so that it could be seen clearly when placed under the microscope. The most important contribution he made was his demonstration that hypodermic injection of a certain quantity of cholera culture that has been killed by heat stimulates the formation of antibodies and thus might possibly produce an immunity to the disease. This discovery—that vaccination of man and animals with *dead* cultures may produce immunity—has been almost universally attributed to two American bacteriologists, D. E. Salmon and Theobald Smith, who in 1886 published their treatise, *On a Method of Producing Immunity from Contagious Diseases.* The honor should go to Cajal, however, since he had demonstrated the same thing in this government report a year earlier.

Certain other points brought out in the report were of importance and were later confirmed by eminent bacteriologists. One of these was the doubt Cajal expressed (later corroborated by Metchnikoff of the Pasteur Institute) that mere inoculation beneath a man's skin with a pure, live culture of bacilli cannot in itself immunize the digestive tube. This doubt was based on the fact that such a culture cannot migrate to the intestines and therefore cannot produce the symptoms of cholera, which is localized solely in the intestinal tract.

As was long to be the case with the work of Cajal, these original contributions passed unnoticed by the men of science of his day. Yet the effort he expended in preparing his elaborate monograph on cholera did not go entirely unrewarded. The provincial government of Zaragoza conferred upon him for his zeal a magnificent Zeiss microscope. His heart bounded with joy at this unlooked-for gift. Nothing could have pleased him better or been more directly useful to the career he was already carving out with firm, deliberate strokes.

His excursion into the study of the comma bacillus awoke in him a profound interest in bacteriology and pathology and he often wondered in later years if it would not have been more fruitful for him, both mentally and financially, if he had followed this path, which was then so fashionable. Histology condemned him to poverty; its greatest reward would be the grudging praise of the few scholars who could understand and appreciate his work. Bacteriology, on the other hand, was unworked soil, full of rich

surprises, inexhaustible in discoveries leading to the relief of suffering and to popular acclaim and honor as one of the mercy-bearers of mankind.

But knowing his own nature, Cajal chose histology, the cautious way but also the tranquil way.

> I knew well that I should never be able to drive through such a narrow path in a luxurious carriage; but I should be happy in contemplating the captivating spectacle of minute life in my forgotten corner and listening, enraptured, from the eyepiece of the microscope, to the hum of the restless beehive which we all have within us.

A more practical consideration influenced him too—the expensiveness of work in bacteriology as compared with the relative inexpensiveness of histology. He envisioned the vast hordes of experimental animals the investigator in pathology would have to buy, feed, and care for, the costly and varied laboratory equipment, the sterilizing ovens, the incubators! For histology one needs only a good microscope and a few standard reagents. So Cajal—now father of four children, earning fifty-two dollars a month—bade farewell, as he puts it, to the alluring microbe and remained faithful to his first love, the cell.

The Regency

Some weeks after Cajal's return to Valencia in October of the terrible cholera year, the king of Spain, Alfonso XII, died after a brief illness—bronchitis—an illness so brief that it had hardly been announced before he was already dead. The value of the peseta fell, and the royal household looked forward with dread to the revolution all felt was sure to follow. To avert this danger, Alfonso's minister, Cánovas, astutely turned over the government to the Liberal Sagasta, who by his appeasement policy staved off revolutionary outbursts. María Cristina of Hapsburg, wife of the dead king (his grandmother of the same name had died a year before Alfonso's second marriage), now became regent of Spain. According to the Constitution, her eldest daughter should have become queen, but María Cristina was pregnant, and in the hope that Alfonso's posthumous child would be a boy, she wanted no steps to be taken in this direction until after the birth of the new baby.

Early in May, 1886, a hurricane swept Madrid, causing great damage to property and widespread suffering. María Cristina, though the time for her confinement was drawing very near, spent her days going about the city giving alms to the destitute and visiting the hospitals, thronged to the doors

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with victims of the disaster. On May 17 her child was born late in the morning. A curious, impatient crowd had been gathering outside the palace since dawn, waiting for news of the birth. Everything hinged on the vital question: a boy or a girl? At high noon a cannon was fired, the flag was run up, and Sagasta came out on a balcony to announce the arrival of a son. The crowd burst into wild *vivas* and promptly dispersed for an orgy of rejoicing throughout the capital. Inside the palace María Cristina was weeping. "Such a pity," she said to those at her bedside, "that my poor Alfonso cannot see this little son, whom he wanted so much!"

Somehow this little child, born a king, drew together the warring factions of his people. And Queen María Cristina was strong enough and diplomatic enough to hold his kingdom for him, though she was only twenty-eight when this difficult task was demanded of her. With the revolutionists adroitly handled by Sagasta, the only threat to her rule came from Don Carlos, rival claimant of the throne of Spain. His followers stirred up a few sporadic uprisings, but the general respect for Alfonso's reign and the sanction given it by the Pope weakened their hope of success. The Republicans were not much of a menace at any time during the Regency, for the memory of the anarchy that had accompanied their short time of power was still fresh in the minds of the people. Besides, the Republicans were divided into rival camps, which could have been united through the great capacities of Castalar, but he had no wish to effect such a union. Upon the birth of Alfonso XIII, then, Spain was more united than it had been for a century. It was a peace and union that lasted during the whole Regency, largely through the skill and intelligence of the queen, who had proved to be a remarkable woman. By the same methods her husband had used so effectively, she continued his work. Even Castelar gave his support to her minister Sagasta. Years later, when her son was to come to the throne, he would find it even more secure than it had been at the death of his father.

CAJAL'S PUBLICATIONS OF THE PERIOD

Upon returning to Valencia in the fall of 1885, Cajal had gone back to his study of living tissue, his enthusiasm for histology not at all tarnished by his recent detour into the more spectacular work with disease germs. During the first three years of the Regency, as the result of months of uninterrupted toil, he published a series of articles on the structure of cartilage, on the crystalline lens of the eye, and on the muscle fibers of insects and of certain vertebrates. But his chief concern at this time was the publication of

an extensive work on histology and microscopic technique, *Manual de histología normal y técnica micrográfica,* the first installment of which had appeared in May, 1884. The next two years were devoted unstintingly to this monumental treatise, which when completed comprised 692 pages of small print and 303 woodcuts made from drawings of Cajal's anatomical preparations by an artist of Valencia. This work was to prove a financial success. (To his amazement, the first edition was sold out and a second edition had to be printed in 1893.) Cajal's motives in undertaking it were fully realized. He gathered together into one volume all his original observations in the field, minor discoveries that had gone practically unnoticed. He disciplined his researches by making them fit into the rigid program demanded by a project of this sort. And, most of all, he satisfied his patriotic wish to show foreign scientists that something original and worth while could come out of Spain, something personal, based on accurate, direct investigation and not a feeble reflection of the scientific productions of other lands.

In these same years, while writing his treatise, which shortly was to become world-famous, he composed a series of popular-science articles for *La ciencia,* a weekly paper published in Zaragoza. These articles were fanciful, lyrical, with imaginative sweep; they gave release, in the midst of his more serious work, to the smothered romanticist in him. They were signed "Doctor Bacteria," the pseudonym he was always afterward to use for his writings in science for the layman. These minor pieces served an important purpose: they showed how fascinating the study of cells and microbes can be and how rewarding, not only in personal terms, but in the contributions to be derived from this practically unknown field for the betterment and enrichment of everyday life. They breathed confidence and a robust faith in the certainty of scientific advance in the years to come. They showed at its full the author's passionate eagerness to probe the mysteries of living things and his exhilaration each time his curiosity gained some slight advantage in its struggle with recalcitrant Nature.

These scientific-literary writings reveal Cajal the man more abundantly than do his more technical works, in which Cajal the master scientist dominates the picture. Here is some of the magic the eye of the microscope unveils, as he describes it:

> . . . the wandering white blood cell, opening a breach in the bloodvessel wall and deserting the blood for the surrounding territory, like a prisoner who files through the grating of his cell; the region of the trachea and the larynx, sown with vibrating hairs, which wave, in response to hidden stimuli, like a field of grain before the wintry wind; the tireless lashing of the sperm cell as it hastens breathlessly toward the egg, the lodestone of its love; the nerve cell, the aristocrat among the structures of the body, with its

giant arms stretched out, like the tentacles of an octopus, to the provinces on the frontiers of the outside world, to watch for the constant ambushes of the physical and chemical forces; the egg cell, with its simple, classic structure, guarding the secret of life, its form like that of a nebula whirling about in embryo innumerable worlds which will emerge in aeons to come; the geometric architecture of the muscle fiber, a sort of complex Voltaic battery, where, as in a locomotive engine, heat is turned into mechanical energy; the gland cell, which in a simple way creates the ferments of our living chemical laboratory, generously consuming its own substance for the benefit of the whole; the fat cells, models of good housekeeping, which in preparation for future famines store up the surplus foodstuffs from the feast of life to utilize them when the organs fail and in the great nutritive conflicts of the body.

Watch these protagonists of the struggle for survival fight it out on their own ground, he urges:

Come with me to the laboratory. There upon the stage of the microscope, tear up the petal of a flower, forgetting for a moment its beauty and its fragrance. Then take a bit of animal tissue; tear it apart without compunction even though it pulsates and trembles at the touch of the needle. Then look through the window of the eyepiece, and the leaf of the plant and the tissue of the animal will reveal to you in every part the same structure—a sort of honeycomb built up of little cells and more little cells, separated by connective substance, and harboring in its cavities, not the honey of the bee, but the honey of life in the form of a semisolid, granular material, encircling a tiny corpuscle, the nucleus.

Now examine a drop of saliva, a few cells from the covering of your tongue, a drop of your blood, the mold found on decaying food—and always the same architecture appears: cells and more cells, more or less modified, repeating themselves monotonously, with wearisome uniformity.

This uniformity in the structure of organic tissues, liquid as well as solid, in the muscle as well as in the nerve, in the stem as in the flower, this precise repetition of the same melodic theme, forms the primordial truth of histology, the basic fact upon which is founded the grandiose and transcendental cellular theory of Schwann and Virchow.

Anticipating the conclusions of later scientists as to the herculean warfare constantly being waged within the body, he continues:

. . . Who will dare to deny that a strenuous rivalry exists in the race among the sperm cells, so that, in order to accomplish the supreme act of fertilization, they hasten toward the egg cell in a throng? Only one of them, the strongest or the most fortunate, will survive the destruction that is inevitable for its more sluggish companions. It alone will tear the mysterious veil in which the ovum is enshrouded, and, losing its degrading tail, will unite with the female nucleus. From this kiss of love will arise its progeny, the cells of the new organism to be born. But only one privileged sperm cell will attain the reward of perpetuating the race and conserving and transmitting, like a new vestal virgin, the sacred fire of life.

Concluding his description of such Homeric conflict, Cajal pointed out, too—a thought stressed by philosophers and biologists whose works he did not then know—that Nature is concerned, not with the life of the individual, but with the preservation of the species.

A single life, however great it may be, even though ennobled by the fires of genius, signifies nothing in the eyes of Nature. That a whole town should be blotted out, that entire races should be annihilated in the struggle for existence, that species formerly powerful should be sacrificed in the battle, matters little to the controlling principle of the organic world. The essential thing is to win, to reach the goal that is the final objective of organic evolution.

To soften the somberness of this picture, he tries to offer consolation for the inexorableness of Nature and of individual death by stressing the immortality of the germ plasm, the eternal substance of living tissue. To most of us this is cold comfort, but it is the best he has to offer:

Let us console ourselves with the thought that if the cell and the individual succumb, the human species, and particularly the protoplasm, are imperishable. The accidental dies, but the essential, that is, the life, lives on. Comparing the organic world with a tree of which the trunk is the original protoplasm, the branches and leaves representing all the species later produced by differentiation and improvement, what does it matter that some twigs are broken off by the storm if the trunk persists with unabated vigor, giving promise of shoots of even greater beauty and luxuriance?

But Cajal himself, commenting on this youthful thesis of his, remarks that it is a gloomy solace to die as a sacrifice to the survival of the species.

Later there is a curious parallelism with the ideas of Schopenhauer and of Herbert Spencer, whom he had not yet read:

This protoplasm filled both space and time with its creation; it crawled in the caterpillar, dressed itself with rainbow colors in the plant, adorned itself with the crown of intelligence in the mammal. It began unconscious and ended conscious. It was the slave and plaything of the cosmic forces and it ended as the driver of Nature and the autocrat of creation. . . .

Whither is life going? Has it reached its limit and exhausted its fecundity in the human organism, or is it keeping in its portfolio plans for still higher organisms, for beings infinitely more intelligent and understanding, who are destined to rend the veil that covers first causes and to do away with all the laborious debates of science and philosophy?

Who knows? Perhaps this demigod, protoplasm, will also die on that sad apocalyptic day when the torch of the sun is quenched, when the embers in the heart of our globe grow cold and its crust is strewn with funereal ashes. Day of horror! Solitude filled with anguish, night of utter darkness, in which the light of the universe, the light of thought, is extinguished! But no. This is impossible. When our miserable planet is worn out and frigid old age has burned out the fire at its heart, and the earth becomes a glacial and barren desert, and the red and dying sun threatens to overwhelm us with everlasting darkness—organic protoplasm will have attained the culmination of its work. Then the King of Creation will abandon forever the humble cradle that rocked His infancy, will boldly attack other worlds, and will solemnly take possession of the universe.

"Forgive me," says Cajal in his mature years, "for these poetic effusions of my youth, which expressed what was then my credo—and I had never

read a word of Nietzsche!" These were to be his only ramblings in the misty domain of natural philosophy.

"EXPORTING TO THE FOREIGN MARKET"

Having finished his fundamental text on histology, Cajal was now eager to match his powers with those of foreign investigators. Only in contest with the strong does one gain strength, he told himself, and he longed to be admitted to the ranks of the leaders in science as urgently as when a schoolboy he had struggled to excel in physical prowess—with many misadventures yet with eventual success. So it was to be again.

The first opportunity that presented itself was through Dr. Krause, histologist of the University of Göttingen, who published a monthly magazine, *Monatschrift für Anatomie und Physiologie,* in which articles appeared not only in German but in French, English, and Italian as well. Dr. Krause had read some of Cajal's writings and asked him to contribute something to his review, promising to pay for the cost of the cuts and to give him fifty copies of the issue in which his article appeared. Cajal sent him two contributions, laboriously translated into French, with a large assortment of drawings he himself had made to illustrate them. The first article was sent directly; the second took him two years to prepare. It had to do with the texture of the muscular fibers of the feet and wings of insects, and became, as he developed it, an extensive monograph with four large color plates. Although it contained some original observations, its interpretations, based on the histological theories of the day, were quite erroneous, as Cajal himself was to demonstrate in his later work.

Having succeeded at last in "exporting his wares to the foreign market," he settled down to a study of the nervous system, the masterpiece of life. He studied it in various animals and in all its several stages of development, guided by the outstanding works in neurology of the period, those of Meynert, Ranvier, Schwalbe, and others. The technical resources of the time, at least so far as they were known in Spain, were quite inadequate for such a study. With the staining methods then at hand, the best preparations showed hardly anything beyond the cell bodies and their nuclei; very little of the long nerve fibers conducting to and from the cell body could be seen. Therefore, even the most zealous investigation left the origin and the terminals of the fibers almost as much a mystery as they had ever been. Yet the structure of the nervous system, chiefly of the human brain, attracted Cajal irresistibly. Many basic questions regarding its function were still unsolved, crying for an answer. The new science of psychology, emerg-

ing dimly at this moment, was demanding exact information on the organization and processes of the brain, without which it could have no truly scientific basis. With it, it was then believed, the whole secret of thought and will would be laid bare.

Cajal's Social Life in Valencia

Cajal's years in Valencia, now soon to come to an end, were happy and full. Though most of his leisure was spent in his laboratory, he did allow himself some recreation with his fellow-members of the Casino de la Agricultura. A group of them would go for hiking trips on Sundays to picturesque districts around Valencia to take photographs of the charming scenes they encountered and to give their muscles free play and much-needed exercise. The constitution of this camera club, which Cajal had drawn up, forbade the discussion of controversial subjects; the talk was always genial, never heated, and on the larger issues of science, art, and literature.

Another form of recreation, though less wholesome, was nevertheless even more absorbing to all its initiates—the practice of hypnotism. Artificial somnambulism and the phenomena of suggestion were all the rage among the scientists in France, and it was inevitable that the contagion should spread across the Pyrenees. In this pseudo-science, the tricks of the so-called witchcraft of the Middle Ages and of theatrical necromancers were unmasked and elucidated in scientific terms.

Love of the marvelous has deep roots in the human mind, even after centuries of science and the slow conquest of superstition. But it was not altogether because of its macabre fascination that Cajal and his friends of the Casino went in for this sort of "black magic" so energetically. To them the manifestations reported from abroad seemed anomalies of cerebral energy that it would be well to investigate, since they might be expected to throw new light upon the workings of the normal as well as the abnormal brain. So Cajal and his colleagues organized a committee for psychological investigation. Their first task was to find suitable subjects. At this point Señora Cajal's patience—a psychic miracle in itself—must have been sorely tried. For their home became a thoroughfare through which drifted a swarm of hysterics, mediums, neurasthenics, and out-and-out madmen. Experiments with this motley crew resulted, as might have been foreseen, in an amazing set of case histories, in which Cajal and his associates had to acknowledge as true many of the strange reports that had come out of France.

To test hypnosis from all possible angles, experiments were also made

on normal people, professional men chiefly. Cajal and his friends, after putting their subjects to sleep, were able to produce, by suggestion, hemorrhages, hallucinations, total or partial forgetfulness of the past and of the subject's own identity, multiple personality, and the remembering of things long since forgotten. The hypnotized persons would perform, after waking from the trance, actions suggested by the hypnotist that were entirely opposed to their normal activities and their natural bent. One patient adjusted his whole life for a week to conform to a ridiculous program outlined for him while he was hypnotized.

Cajal was quick to see the curative possibilities of hypnosis and straightway tried them out. He claims to have performed feats in this field quite comparable with those of the miracle-workers of the past. He was able instantaneously to turn the gloomy moods of depressed persons to joyous ones, to cause patients who had a phobia against eating to eat normally, to enable those hysterically paralyzed to walk again, to cause patients permanently to forget painful memories that were torturing them and making them ill, and even in one woman to produce by hypnotic suggestion complete insensitivity to the pains of childbirth.

Naturally his fame as a wonder-worker was spread abroad and his once peaceful home continued to be inundated with a throng of unbalanced people, some of them quite insane, begging him to cure them. (In the midst of all this, there was a new baby to care for, little Enriqueta, born in 1886.) Cajal helped as many of those who came to him as he could, without recompense, and then withdrew from the practice, his curiosity now satisfied. The only things that he was never able to fathom in this detour into hypnotism were the ability some of the subjects showed while in the hypnotic trance to see through opaque bodies, the transference of a sensation to the wrong sense organ, and mental telepathy. At spiritualistic séances, when this doubting Thomas visited them, the medium's skill seemed to melt into air thinner than her ectoplasm. What astonished him most in these sessions was not the supernatural manifestations, for none took place, but the gullibility of the audience, who interpreted as communications with spirits certain nervous phenomena of the medium or the influence of their own habitual thought patterns or the theatrical tricks devised to produce an eerie effect. Cajal would go away from the séances saddened by this pathetic suggestibility of the human mind, which he called "an enormous defect in our structure, by which even the most outstanding intelligence may on occasion be converted by skillful suggesters—orators, politicians, soldiers—into the humble and passive instrument of madness, ambition, and greed."

The Activity of the Embryonic Human Heart and Its Significance for the Understanding of the Heart Movement in the Adult*

WILHELM HIS, JR.

I. Introduction

IN the work printed above [Studies on innervation of the heart] Romberg and I presented proof that the ganglion cells of the human heart belong to the sympathetic system and that they reach their destination by wandering out from the spinal ganglia. We pointed out that the sympathetic ganglionic elements are differentiated from the spinal ganglia by definite characteristics and that, in great probability, a sensory function must be ascribed to them since no proof of their motor function can be furnished.

The experiments of Fano and Wooldridge especially lead to the conclusion that the heart beat must be independent of the presence of nerve elements to a much greater degree than has heretofore been assumed. We expressed the decided belief that the ganglia of the heart are part of the regulatory mechanism, whereas automaticity must be considered as a part of the heart muscle. However, it seemed necessary to obtain further proof on human embryos, and the pursuit of a useful object for investigation would go hand in hand with this.

Thus I came to investigate in a systematic manner the development of the cardiac nervous system in the various vertebrates. This work is printed in detail in the *Abhandlungen der Kgl. Sächsischen Gesellschaft der Wissenschaften,* Bd. XXXI. Heft 1. Here it is only necessary to present in very brief form the most important items given therein.

All of the sympathetic ganglion cells of the head, neck, thorax, and very likely also lumbar and pelvic regions, arise from the sensory ganglia, that is, the ectodermal portion outside of the medullary tube from which the anlage of the above-mentioned ganglia also arise. In the form of loose swarms, they migrate through the embryonic mesoblastic web, in which they prefer to make use of those paths along which existing blood vessels and nerve trunks lie.

* Translated by T. H. Bast and Weston D. Gardner, Madison, Wisconsin, from *Arbeiten aus der Medizinische Klinik zu Leipzig,* 1893, 14–49.

They become anchored in that they become surrounded by a mesoblastic membrane, that is, the neurilemma; also in that they find a place to attach on a serous membrane or an organ margin through which they are not capable of breaking. Then they spread along such a surface until with increasing age their faculty of movement comes to an end.

During the period of migration the cells also multiply so that they present the picture of nervous germ cells.[1] During this migration, or after its termination, the cells develop a protoplasmic process which may be directed toward the peripheral organ or towards the central organ. Its further lot has not yet been fully investigated. It branches in some cases in a T-form and appears to end, in part, in the organs (Smirnow, Arnstein), and, in part, in the neighborhood of other sympathetic cells or spinal ganglion cells in a tree-like branching (Ramón y Cajal).

The sympathetic ganglion cells of fishes and amphibians remain, to a large extent, unipolar; those of birds and mammals sprout a number of shorter, branched processes later on, which are like the protoplasmic processes of brain and spinal cord cells and, like them, probably mediate stimulation from one cell to another.[2]

The formation of the white chain occurs in the following manner: at first, out of the crossing of the ventral and dorsal spinal roots, the rami communicantes emerge and unite themselves into a longitudinal commissure which secondarily takes up the sympathetic wandering cells.[3]

Ganglion cells and cerebrospinal nerve fibers penetrate into the organs almost at the same time, but the former ones first; the nerve fibers, which have emerged from the cells, attach themselves to the latter so that each nerve going to an organ which is equipped with sympathetic ganglia must be of mixed nature, partly sympathetic, and partly cerebrospinal.

The nerve fibers and ganglion cells which innervate the heart enter it along the larger blood vessels. Because of the positional relationship of the heart to the mouth cleft and the head ganglia, it follows that in fishes and amphibians the entrance occurs only along the trunk of the superior vena cava; thus the largest and earliest ganglionic masses are formed at the sinus venosus whence the nerve trunks and cell groups proceed toward the atria and ventricle.

In the chicken, as well as in man and the cat, the entrance occurs along the arteries. In the space between the aorta and the pulmonalis, there arises the bulbar plexus which sends out the coronary nerves. Later, along the veins, other nerves and ganglion masses appear in the region of

the sinus venosus and the posterior wall of the atria. They form the auricular plexus which becomes united with the bulbar plexus by means of a uniting plexus which passes behind the sinus transversus pericardii. The main results of this work lie in the observation that the ganglion cells do not arise within the heart but, at a given point in the development, arrive there from outside of it.

Haller[4] had already indicated that, in the incubated chicken egg, the heart of the embryo began to beat at a time when no other tissue was excitable; and Bischoff[5] had concluded that, because of the prolongation of the embryonic heart beat outside of the maternal body, the final cause for the activity and even for the rhythm of this activity must be sought for in the heart muscle.

Eckhard[6] sought the solution of the question of heart movement in the observation of embryonic hearts and pointed out that it begins to beat before its elements have taken on the character of true muscle cells. Preyer[7] mentioned, in discussing the activity of the embryonic heart, that the heart beats even before there is the slightest trace of nerve elements or muscle fibers.

All of these observations lack sufficient proof. One could postulate that the ganglion cells were already in the heart even though they could not be demonstrated, and this point of view was all the more reasonable since, before the discovery of the migration of sympathetic cells, the various authors[8] knew no other way than to consider the ganglion cells as having their origin within the organ itself. And just as the immature embryonic heart cells are capable of contracting, so it is possible that the immature ganglionic elements are capable of displaying their motor activity, a concept which was not contradicted by sufficient truth.

With the exact determination of the time in which the heart receives its first innervation, proof is furnished that every movement of the embryonic heart which occurs before such innervation exists must arise from the embryonic heart muscle. From this point of view the investigation of embryonic heart activity assumes a basic meaning and we may be permitted to attempt to indicate from it the explanation of heart movement in the adult.

II. Structure and Function of the Embryonic Heart

The heart of the chicken embryo (on which most of the observations have been made) develops, as is known, out of a right and left half which

occur as groove-like anlages which, during the formation of the foregut, approximate each other and unite to form a tube, in which one can differentiate a rostrally directed arterial end and a caudally directed venous end. As soon as the tube is formed it begins to pulsate, in the chick the first pulse occurring at about thirty-six hours after the beginning of incubation.[9] At first the pulsations are irregular, this being accounted for by the cooling which occurs in opening the egg; by the end of the second incubation day they are regular; their frequency depends on the temperature and decreases when the heart begins to die off.

On the third incubation day, the heart tube has the form of an S-shaped loop in which the divisions of the developed heart already can be recognized. The outer or caudal end receives the veins: it later corresponds to the sinus venosus. The first segment of the S is flattened and possesses two half round projections, the later heart ears. It represents the auricular part of the heart. In the second part of the bend one can recognize an arterial and a venous segment besides a communicating piece; the latter passes later over the ventricle and separates itself, by means of a slight notching, from the arterial segment (the aortic bulb) as well as from the venous segment (the canalis auricularis).

In the course of the fourth and fifth incubation day the transformation occurs which determines the eventual splitting of the heart. By means of the approximation of the arterial and venous ends the auricle comes to lie above the ventricle (die Basis des letzteren horizontal gedacht). The heart ears surround the aortic bulb from left to right.

The part between auricle and ventricle, the ear canal, becomes surrounded by ventricle and telescopes itself, as a double-walled muscular funnel, into the inside of the chamber narrowing the atrioventricular ostium, and externally outlines the coronary groove. On the inner free rim of the funnel, by means of the growth of the endocardium, there arises the so-called endothelial cushion or atrioventricular lips, which operate as temporary atrioventricular valves to close the ostium during ventricular systole.

Between the fourth and fifth day the muscle wall of the heart also changes. The cells, which up till now had been blister-like, take on a fibrillar structure, and on the inner wall of the chamber there appears the net-like arrangement of the trabeculae.

From this time on, there occurs also a change in the character of the heart contractions. Heretofore, it occurred in the form of a peristaltic wave with uniform speed over the entire heart tube. Now it begins at the

vena cava, proceeds with a slight hesitation onto the auricles, then, after a slight pause, the entire ventricle contracts and finally the peristaltic movement passes out at the aortic bulb.

Thus, on the fifth incubation day, the contraction occurs the same as in the adult fish and frog. If one discounts, now, the isolated movement of the bulbus, which in mammals loses its musculature, and that of the sinus, which is incorporated into the auricle, then the contraction form is identical with that of the adult birds and mammals.

I am convinced from numerous repeated observations that, up to this time, the heart has no ganglion cells. These first appear on the sixth day, in the space between the aorta and the pulmonalis, and have not the least influence on the course of cardiac contraction, as can be determined by the ablation of the aortic bulb with its ganglia. These facts prove irrefutably:

1. That a nervous coordination center is not necessary for the course of cardiac contraction, even as it occurs in the adult;

2. That the occurrence of a pause between auricular and ventricular contraction is determined by the structure and arrangement of the musculature and not by the hesitation of the conduction of the impulse from a ganglionic complex (Marchand).

The development of the heart in other vertebrates proceeds in a similar manner as heretofore described for the chick. In the shark, trout, frog and rabbit, I can say with certainty that the appearance of cardiac contraction precedes the ganglia; that this occurs in a similar manner in man appears from the observation of Pflüger[10] who observed the beating of the heart in an embryo of three weeks. The first ganglia in man do not appear until the end of the fourth week.

So far as observations have been made, the heart in all vertebrate embryos beats as soon as a tube is formed, at a time when the development of the spinal ganglia has not yet reached the stage of migration of the sympathetic cells. We can thus add the following to the abovementioned statements:

3. The heart beats in embryos of all vertebrate classes without the help of motor ganglia.

In attempting to carry over the embryonic observations to the adult one encounters a difficulty which here will require a careful analysis. In the embryo the vein, auricle, ventricle, and bulb form a continuous muscle sheet. This, in the course of subsequent development, becomes interrupted at the boundaries of the individual parts of the heart. It is

not the same in all vertebrate classes. The atrioventricular boundary in the fishes (Fig. 1) is like that in the embryo; that is, the auricular wall passes over into the telescoped-in atrioventricular funnel and this is in immediate relationship to the musculature of the ventricular basis. I am not in the position to say whether the muscle bundle of the one part passes over into that of the other; in all events, they abut each other most intimately without an intervening membrane. A pericardial connective tissue sheet pushes in between the two walls of the atrioventricular funnel but does not reach its inner margin. It exists without hook-up with the actual valves, the latter resembling the endothelial cushions of the embryo as growths from the endocardium at the base of the atrioventricular funnel.

In the frog (Fig. 2) the connective tissue sheet of the pericardium, in contrast, pushes so far between the two muscle walls of the funnel that it separates them at its free tip. Thus, the outer sheet unites with that of the ventricular basis; the inner, in contrast, which in an early stage united with the trabeculae of the ventricles, forms thus an intimate continuation of the muscle of the auricle with that of the tip of the ventricle.

The actual valves in the frog are attached to the base of the funnel as a purely endocardial growth. The atrioventricular ganglia are closely associated with them and the funnel. It is thus, as Gaskell[11] has mentioned, that in the attempts of Engelmann and Marchand to cut out the atrioventricular ganglia the union of the auricle and ventricle was damaged at the same time. When Gaskell repeated this procedure, without disturbing the muscle sheet, the progression of the heart beat onto the ventricle was not disturbed.

In birds and mammals (Fig. 3) the pericardial sheet breaks through both walls of the funnel at its tip so that the inner lamina has no union with the papillary muscles. The valves of the atrioventricular opening, at a certain period of time, consist of five independent sheets: namely,

1. The endocardial plate, with its endothelial cushions, which is directed toward the auricle;

2. The muscle wall of the funnel which is directed toward the auricle and which is continuous with the musculature of the auricle;

3. The ingrown lamina of the pericardium which in the adult forms the chief mass of the valve sail;

4. The under or ventricular lamina of the funnel which is continuous with the papillary muscles;

Fig. 1. Frontal cut through the heart of a shark (Mustelus laevis, newborn). Magnification 10. *V* Ventricle, *Vh* Auricle, *B* Aortic bulb. *S* Aortic valves. *A-A* Atrioventricular valves. *Tr* Atrioventricular funnel. The muscle is indicated by lines and the connective tissue by dots.

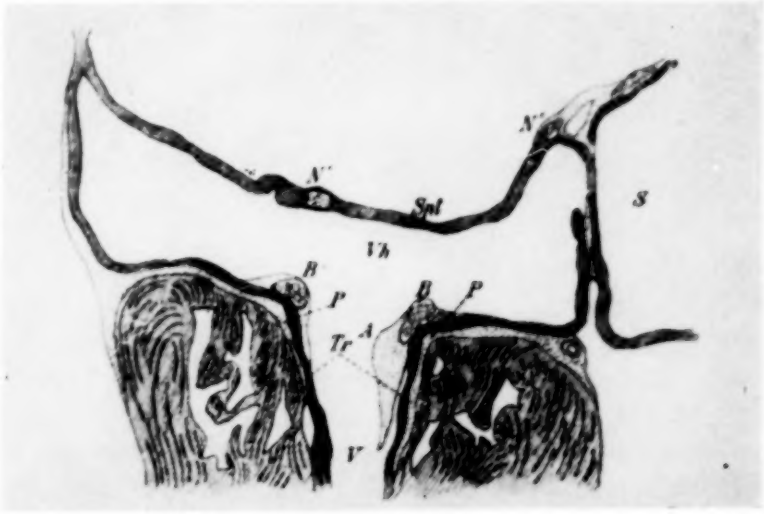

Fig. 2. Sagittal cut through the heart of a full grown frog. Magnification 15. *V* Ventricle. *Vh* Auricle, *Spt*. Auricular septum. *S* Sinus. *A* Posterior atrioventricular valve. *Tr* Atrioventricular funnel, whose cross-sectioned circular bundle is indicated by rings. *P-P* Pericardial plate of the funnel. *B* Bidder's ganglion. *N'N''* Anterior and posterior nerves of the septum. Muscle and connective tissue are indicated as in Fig. 1.

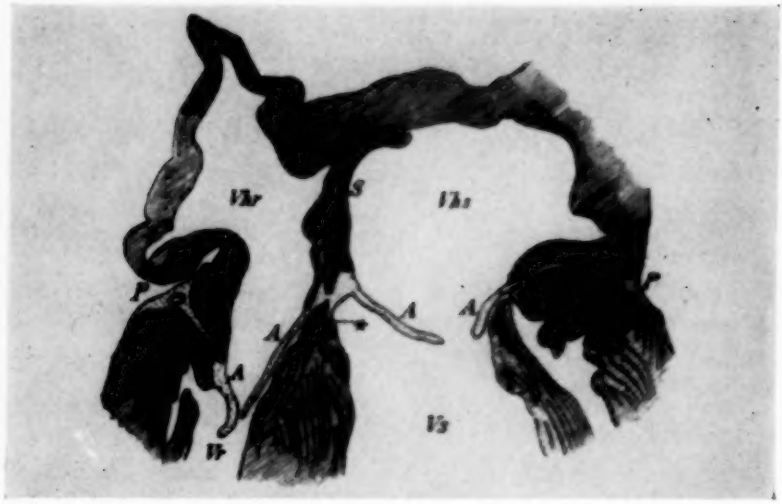

Fig. 3. Frontal cut through the heart of a grown mouse. *Vr, Vs* Right and left ventricle. *Vhr, Vhs* Right and left atria. *S* Auricular septum. *Ss* Ventricular septum. * Conduction bundle. *A-A* Atrioventricular valves. *P-P* Pericardium of the coronary groove. Muscle and connective tissue indicated as above.

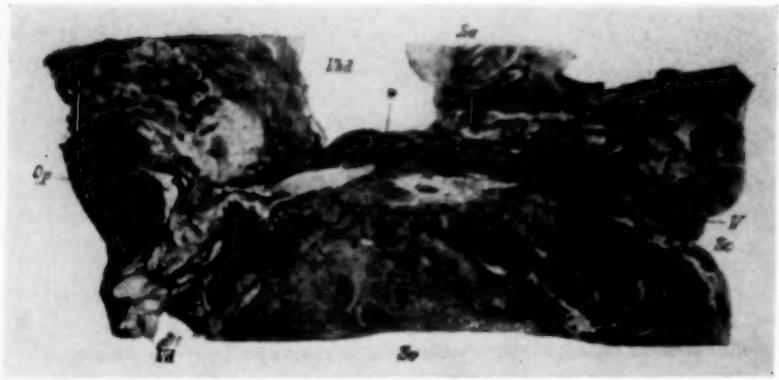

Fig. 4. Sagittal cut through the atrioventricular boundary of the heart of a newborn human baby. Magnification 7.5. The ventricular septum is shown in its entire length, the atrial septum in only part of its length. *Vhd* Opening of the right auricle. *Vd* Opening of the right ventricle. *Sv* Ventricular wall. *Sa* Auricular septum. *Sc* Coronary groove. *V* Coronary vein. *Op* Pulmonary ostium. * Conduction bundle.

5. The ventricular endocardial lamina.

Both muscle laminae degenerate gradually, the ventricular one first, which, together with the tips of the papillary muscles, goes over into connective tissues (chordae tendineae). The other, the one adjacent to the auricle, degenerates later and then only partly; the remnant forms the muscles of the valves which Kürschner[12] discovered, Joseph[13] described, and Darier[14] carefully investigated. One was thus forced to accept the fact that there could be no muscle continuity between the auricle and the ventricle. This was the basis for McWilliam's belief[15] that the help of nerves in carrying the excitation from auricle to ventricle could not be dispensed with.

After long search I have succeeded in finding a muscle bundle which unites the auricular and ventricular septum, and which, up to now, has escaped observation because of incomplete exposure, for it is visible in its entire extent only when the septa are cut exactly in their longitudinal direction. From such cuts, as well as in serial sections, I was able to recognize the course of the bundle and have demonstrated it in a grown mouse, a newborn dog, two newborn and one adult (30-year-old) human (Fig. 4). The bundle arises from the posterior wall of the right auricle, near the auricular septum, in the atrioventricular groove, attaches itself along the upper margin of the ventricular septal muscle by means of numerous fiber exchanges; proceeds on top of this toward the front until near the aorta it forks itself into a right and left limb which latter ends in the base of the aortic cusp of the mitral valve.

Whether this bundle really transmits the impulse from the auricle to the ventricle I am unable to say with certainty since, up to now, I have not attempted any transection experiments of it. Very likely its presence is an argument against the belief of those who, because of the lack of muscular continuity between auricle and ventricle, seek to prove the necessity of nervous conduction.

That in mammals the coronary nerves have no part in this conduction is shown by the experiments of Wooldridge[16] on dogs. In these animals the ventricles are exclusively innervated by the coronary nerves which alone could bring about this movement. Following their transection, the auricle and ventricle continue to beat in the same tempo; if, on the contrary, with the anterior ventricular nerves intact, the wall of the auricle was crushed, then the ventricle and auricle continued to beat but each in its own peculiar time.

The investigations of Tigerstedt[17] appear to give a proof against the

conduction in the above-mentioned bundle. When Tigerstedt made puncture holes from left to right through the septal wall the progression of the beat in the ventricle was not disturbed. But Tigerstedt's stab was made above the atrioventricular groove; the bundle in question arises within it and in its course approximates the apex more and more so that, by that attempt, it was not destroyed. Besides this there is no basis why, through partial clamping of the auricles whereby a bridge of about six millimeters remained standing at the posterior surface of the auricle as well as by total clamping, the rhythm of the ventricle is disturbed. In the manner in which Tigerstedt carried out his ligature, it comes to lie higher than the muscle bundle, separating thus the auricular remnant from the main mass of the auricle, but can give no information as to the separation of the bundle from the ventricle. Even though we have to admit that the way which the impulse takes in its passage from the auricle to the ventricle is not known with certainty, nevertheless we can determine its probable course by exclusion. For neither in the frog, turtle[18] nor dog (Wooldridge) is the rhythm of the ventricle disturbed when the nerves to it are severed. The experiments of Tigerstedt have proved that the stimulus of blood flowing into the ventricle did not bring about its contraction. If we do not wish to take refuge in too hypothetical concepts, there remains the course of conduction from muscle to muscle as it is unquestionably known to exist in the embryo. Whether the described bundle or those little bundles seen by Romberg (in the hearts of newborn rabbits, which extend from the auricle to the ventricle at the base of the atrioventricular valves, and whose existence in the adult animal up to now has not been investigated) are the pathway, is a question which for the time being must remain open.

There is now a further question to be answered: whether for the adult heart it is necessary to have nerve centers to bring about coordination. That these are not necessary for normal heart movements, as Johannes Müller and Volkmann believed, is apparent from the fact that the movement in the embryo occurs without a center.

The remaining proofs for the existence of a coordination center are not of a kind which can command unqualified recognition.

Aubert and Dehn[19] found that potassium salts called forth unregulated lively movements (delirium) of the heart. They concluded, since the movement continued over a long period, that it was not to be considered a paralysis of the heart muscle, but rather of the regulating central organ—an ataxia. If this were right, then an excised piece from

the ganglion-free tip of the heart could never beat other than in an unorganized manner, since it lacks such nerve centers. Numerous investigations teach, however, that under suitable conditions they are capable of beating regularly and rhythmically.

Kronecker and Schmey[20] observed a fibrillation and diastolic standstill of the ventricle when they injured a spot not definitely located at the lower margin of the upper third of the ventricular septum. They considered this spot as the crossing point of the innervating paths which normally serve as the coordinating centers for the musculature of the ventricle.

Germain-Sée and Gley[21] confirmed the observations of Kronecker in the rabbit, succeeding three times out of fourteen attempts. They considered the injured spot not as a coordination center but as an acceleration center, which when stimulated causes paralysis through excessive muscle movement. Both hypotheses lack an anatomical basis. In the ventricular septum are neither nerve trunks from the auricle to the ventricle nor ganglion cells. Since delirium cordis can also be evoked in the dog through faradic stimulation, puncture wound and cutting in other parts of the ventricle,[22] it appears to me that Kronecker's results lay in considerable injury.

The investigations thus far carried out show that it is not necessary to accept a nervous organ for the conduction of the impulse from the auricle to the ventricle and for the coordination of heart movement, even for the adult animal. In this direction, then, there is no obstacle in the way of transferring the observations on embryonic heart activity to the heart of the adult animal.

Let us turn back to consider the embryonic heart. Fano[23] carried out the experiments of Stannius on the heart of chicken embryos on the third day and reached the surprising result that the venous end of the heart tube reacts differently than the arterial end. He exposed the heart by cutting into the body of the embryo from the rear, at the level of the atrioventricular opening between the arterial and venous segment, and fixed the two body ends. Through slight traction he obtained the heart as a more or less bent tube whose movement he registered photographically.

He could measure the progresison speed of the peristaltic wave and determined it to be from 3.6-11.5 mm. per second. He observed that the wave arrived at the small curvature of the tube earlier than at the larger and found that the time difference (6-8 hundredths of a second) corre-

sponded approximately to the length difference. Thus the hypothesis of Preger and Wernicke, which considered that the impetus for contraction was determined by the pressure of the inflowing endolymph, was disproved. The heart could be kept beating for two hours outside of the egg by maintaining the incubation warmth. Before death set in, the pulse passed from a regular to a periodic and finally to an irregular form.

When Fano severed the heart tube into two parts by means of a cross cut in the region of the atrioventricular boundary, the auricle continued to beat in an accelerated tempo; the ventricle stood still and gradually, after a longer period of time, began to beat, but the number of contractions was less than that of the auricular half. A single stimulation of the ventricular part at standstill produced a return of the rhythmic contraction for a long time.

When the atrioventricular boundary was crushed but not transected, the ventricle also stood still but after a time began to beat so that for every three to four beats of the auricle one occurred for the ventricle. Gradually it returned to the pulse frequency of the auricle even though the crushing was still apparent as a visible groove. When the separation was performed closer to the ventricle, the excised piece was stationary, whereas the piece of the ventricle which hung onto the auricle beat synchronously with it. By warming up the inactive piece, the rhythmical beat could be reinstated.

If the separation took place above the atrioventricular groove, the piece of the auricle which hung onto the ventricle was sufficient to cause the ventricle to contract. When Fano separated the heart by means of three cuts or more, pulsation occurred in all segments after a while and the frequence of the beat was greater in the piece closest to the venous end.

In response to the stimulation by induction current, the ventricle was much more sensitive than the auricle. When the heart was transected and the two pieces were fastened down at some distance apart, if a current was led through the auricular piece, one strength of induction beat was sufficient to bring the ventricle into pulsation but did not influence the auricle. From these experiments Fano drew the following conclusions: "Heart movement is an automatic characteristic of the embryonic heart muscle. Within it reside two properties, the one being automatism and the other excitability. The auricle is primarily the seat of automatism, the ventricle that of excitability." Fano thus emphasized the autom-

atism of the venous end of the heart for, if the heart movement was a symptom of irritation, then it would have to have its origin in the most irritable part, the ventricle, and by transection would be maintained in it only.

In order to determine whether the greater resistance and greater persistence of the auricular heart beat depend upon a better respiratory capacity, Fano exposed either the entire embryonic heart or the transected heart to various types of gases. Oxygen temporarily increases the beats; hydrogen slowly diminishes them up to a complete standstill; carbon dioxide increases them at first, then decreases them; carbonic acid diminishes the number of beats and the irritability up to a point of standstill. With the initiation of the damaging action in all cases, the ventricle ceases its action first, followed by the auricle. The irritability ends later than the automatic activity and this peculiar characteristic appears: that, with the loss of irritability, faradic currents can be passed through the heart without producing damage. These currents, if sent through an irritable heart, immediately cause its death. When the damaging gases are displaced by air or oxygen, movement in the auricles returns first, followed by that of the ventricles; in these cases the irritability returns earlier than the automaticity.

Fano concluded from this appearance that the functional superiority of the auricle over the ventricle depends on the greater affinity of the auricular tissue for oxygen and the greater capacity for storing it. I have carried out Fano's transection experiments and can verify them in all points.

In order to test the difference between the auricular and ventricular parts more carefully, I subjected the embryonic chick heart, of two to six incubation days, to the action of various poisons. I used an apparatus for observation which in all respects was similar to the one used by Fano and, like him, made photographic registrations of what happened. If the heart is protected from dehydration and has taken on the temperature of the incubation chamber, the frequency of its movement is constant for a time. Then it gradually diminishes and, after one to two hours, passes over into arrhythmia, finally stopping entirely. The irritability for mechanical and thermic stimulations surpasses that of the spontaneous pulse.

One can expose the heart either as Fano did or better (because it is much less damaging) the entire embryo with its vascular bed can be

removed from the egg and, with yolk side up, can be brought in contact with the poisons. Transection experiments can be carried out only on the exposed heart.

Atropine sulfate, in 1-5 percent solution, applied to the vascular bed (area vasculosa), does not change the beat rate in a noticeable manner. One to two drops of 1 percent solution, applied to the exposed heart, produces standstill. If the auricle and the ventricle are separated by a transection, the latter comes to a standstill first, but is soon followed by the auricle without preceding slowing.

Muscarine (prepared from choline), painted on the area vasculosa, produces a standstill several minutes after application, after the poison is absorbed and carried with the blood to the heart. After some time, during which the poison has distributed through the entire blood mass, the effect passes away without leaving behind a prolonged slowing.

On the exposed heart, one drop of 1 percent solution produces a momentary standstill. As the poison is gradually removed, the pulse frequency gradually approximates the earlier pulse rate. A second and third drop produces a standstill which is not overcome by atropine.

In the severed heart, the first drop of muscarine solution (0.5 percent) acts markedly to slow the ventricular pulse whereas the auricle continues unchanged. A second drop stops the ventricle, the auricle continuing to beat with a slight slowing. Only large masses of muscarine bring about auricular standstill. In one attempt the superior and inferior venae cavae continued to beat in a very lively but uneven tempo.

Nicotine, in 0.1 percent solution, produces a slight acceleration of the pulse. In a 1 percent solution, applied to the exposed heart, a strong slowing occurs in which the duration of the systole seems prolonged. Nicotine, when applied dropwise on the exposed heart, does not act in a uniform manner. Several times I could observe that the pulse of the ventricle increased and that of the auricle decreased. In other cases it drops from the very beginning; standstill finally follows, usually in the auricle before the ventricle.

A digitalis preparation (Digitalinum verum Böhringer, for which I thank Professor Böhm) quite markedly increases the frequency of the auricle and, nominally, that of the ventricle even in a 0.05 percent solution. Stronger solutions increase the ventricular beat rate to 170-180, the accompanying contractions becoming ever shallower and finally unnoticeable. In this condition the ventricle as well as the bulbus is strongly contracted and completely unresponsive to mechanical stimulation. Dur-

ing this, the auricle beats on with increasing frequency and presents a characteristic picture. The contractions begin simultaneously at several points, spreading through the surfaces in various directions, to result in a heaving and wallowing which realistically reminds one of delirium cordis.

A very peculiar fact is that hearts under a lower temperature are unresponsive to the action of even very concentrated poisonous solutions.

The poison experiments in the embryo present considerable difficulties. The frequency of the heart is, to a large degree, dependent upon the temperature and changes with the slightest variation. Thus it is constantly and uniformly reduced as soon as the embryo is removed from the egg.

Therefore, one can carry on the experiments only with the larger masses of poisons which produce their results rapidly and strongly. Thereby many of the more delicate changes and observations are lost. One sufficient observation, however, results from these experiments. It is the difference of sensitivity of the auricle and ventricle in response to the poisons. Muscarine, atropine and digitaline produce their disturbing action in a higher degree on the ventricle; regarding nicotine, it appears as if it brought the auricle to a standstill earlier than the ventricle.

If the substance of the two parts of the heart were similar, then the part which is most rapidly infiltrated by the poison would respond to the intense activity of the poison, and that is the thin-walled auricle. The majority of the poisons, however, show their effect upon the ventricle, and we must conclude therefrom that the substance of the ventricle (with the greater excitability and lesser resistance to poisons) reacts differently towards the poisons than that of the auricle. If Fano believed he had found a basis for this difference in the differing affinity for oxygen, then this can no longer be considered valid in face of the poison experiments. There remains, thus, only the concept that from the beginning *the physiological characteristics of the individual parts of the heart of the embryo are different.*

The appearance of ganglia in the heart does not apparently change its characteristics; at least, the heart of a seven-day chick behaves the same as that of a five-day chick. It is altogether questionable whether the ganglia are capable of functioning immediately after their appearance. They require for that a hook-up with other ganglion cells, cerebrospinal nerve fibers, and the muscle cells. The end-apparatus, which is unquestionably necessary for this function, arises later. Ramón y Cajal

first showed fully formed sympathetic cells in the white chain of the chicken on the 14th day. (That the vagus excitability in mammals becomes active only shortly before birth may be dependent upon this same cause.) Older chicken embryos are not suitable for further experiments. From the 8th to the 9th day on, the heart is supplied with blood through the coronary arteries. If the circulation in these arteries is injured, through cutting or through unavoidable disturbance of the blood vessels of the yolk, the heart becomes asphyxiated exactly as in a grown bird or mammal. Introduction of artificial circulation is hardly possible because of the friability of the embryonic heart.

The variations in the physiological characteristics of the arterial and venous parts of the heart, which Fano discovered, presents the key to the understanding of the regulated course of cardiac contraction. Movement always arises from the point possessing the greatest beat rate; contraction waves progress from it through the entire heart. They cover the automatic characteristics of the less rapidly beating parts, these first becoming manifest when, through transection or crushing, the influence of the most automatic part is destroyed.

Since we carry over to the adult heart the differences between the sinus, auricle, and ventricle which were found in the embryo, we may ask ourselves the question: whether, with the help of this hypothesis, an explanation which is more satisfactory than those which heretofore have been indicated presents itself for the observed movements in the adult as well as in the experiments of Stannius. To answer this question it is necessary to examine the teachings of heart movement in their historical setting, and to re-examine the reasons, mentioned previously, for the existence of motor heart ganglia.

III. History of the Knowledge Regarding Heart Movement

The opinions of physicians who lived before Haller's time may be passed over here in spite of their great interest, since they are based in general on altogether too primitive observations and experimentation. The teaching of Haller, in contrast, should receive our attention all the more because in many respects it is contrary to our concept but in other points coincides.

Because of the fact that the excised heart continues to beat, Haller[24] declares that it was impossible to believe that it could receive its stimulation for movement from the central nervous system. Even the nerves

within the heart may not be considered as the reason for this movement, since in the chick embryo the heart beats at a time when nerves cannot be stimulated. The source for this rhythmic movement must lie in the heart substance which is capable, through its irritability, of answering a stimulus by means of a contraction. Haller looked for the stimulation in the movement of the blood. When the blood streams into the auricle it is stimulated to contraction. The blood is then drawn into the ventricle where it produces a second stimulation. Thus the explanation is apparent, that in the heart beat the auricle contracts first, followed after a pause by the ventricle.

The teaching of Haller found divided acceptance. The impossibility of considering the blood movement to be the reason for the activity in the excised heart was too apparent not to require contradiction. The critics divided into several camps. The one, in spite of Haller's contra-indications, placed the source of stimulation of heart movement in the spinal cord and oblongata. The last adherent of this concept, Legallois, was conclusively contradicted by Wilson Philip in 1822. Others sought the reason for the heart beat in the motor power of the N. sympathicus. A remnant of this, which remains in the nerves of the heart after excision, is sufficient to maintain the movement of the heart for some time.

Felix Fontana,[25] in general an adherent of Haller, threw overboard the latter's concept of stimulation through the blood and set up the hypothesis that the heart muscle during contraction lost its irritability but that "in relaxto musculo aliquem stimulum videri superesse qui sensim increscat et demum sufficiens robur nactus in contractione erumpat" (the sensitivity can be considered to increase in relaxed muscle until it becomes sufficiently strong to burst into contraction). One sees that this is the idea which, more than a hundred years later, found experimental confirmation in the work of Bowditch, Marey and Lowén.

Among his contemporaries Fontana found no adherents. The majority turned their interest to the N. sympathicus and no one less important than Johannes Müller[26] sought the basis of heart movement in the characteristics of this nerve.

Accepting an example given by Reil, J. Müller compared the ganglia woven in between the nerves going to the heart with electric batteries; he ascribed to them the characteristics of storing the transmitted stimuli sent to them, periodically(just like an electrical discharge) giving it off to the heart. That the excised heart can continue its beat proved to him the specific influence of the nerves remaining in the substance of the heart

which appeared to be the last source of contraction; that it died off, after a time, however, lay in the lack of the living influences of the brain and spinal cord. The constant source for the contraction is *primo loco* the motor power of the N. sympathicus, but the reason for the preservation of this latter and its stimulation is the brain and the spinal cord. For the explanation of the course of the contraction he considered a contemporary aid by the ganglia of the heart substance.

In 1844 Remak discovered the ganglia in the auricle of the calf heart. Therewith the interest was directed to these elements and one sought in them the nervous center from which the heart movements originate and are regulated.

Volkmann[27] was the keenest adherent for this point of view. If one severs the heart into several parts, that part which was stimulated contracted. If one stimulates a given part of an undamaged heart, under all circumstances the pulsation starts at the sinus and progresses to the auricle and, finally, the ventricle. Thus cardiac contraction could not be a stimulation movement but rather a planned, regulated movement process. Such a process requires a center from which the timely course of the movement can be directed.

The muscle elements of the heart are not considered a substrate for that kind of center. One has thus to choose only between the nerve fibers and the ganglion cells which are present in the heart. The sum total of physiological experience speaks for the latter choice.

Volkmann's evidence, sharp and brilliantly presented, pointed with such compelling necessity to the motor nature of the ganglion cells of the heart that doubt did not seem possible even though, with many limitations, these structures have played the leading rôle in the teaching of heart movement up to recent times. The weakness of Volkmann's theory lies in that it placed heart muscle, with its peculiar characteristics, without modification on an even basis with skeletal muscle, which appeared all the more unbelievable since the characteristic forms of its elements and their hookups with each other were not yet known.

A basis for the error lay in the choice of the objects for investigation. Volkmann used, as did most of his followers, the heart of the frog. Though momentarily convenient it has a drawback which, in the experiments regarding heart movement, has played an unfavorably dominant rôle.

By means of a unique procedure during development, the nervous structures of the frog, which in every other vertebrate approached the

heart from the outside, reach the inner part of the septal wall, for example, the inner surface of the atrioventricular valves and the ventricle. As a result of this deep position, stimulation and destruction of the nerves and ganglia are not possible without extensive damage to the muscle.

Through the experiments of Ludwig, Bidder and Dogiel and others, we have learned the course of the cardiac nerves in greatest detail. We learned that they arise from the vagus and proceed along the superior vena cava to the organ, forming a plexus richly supplied with ganglion cells at the vena cava sinus. Two branches, also ganglionated, pass from this plexus through the auricular septal wall to form two large, ganglion-containing masses on the atrioventricular valves, radiating from there onto the inner surfaces of the ventricle. In the heart at least the lower two-thirds of the ganglion-free ventricle can be contrasted with the ganglionated auricle and sinus. Since physiological differences have been discovered between these parts, one has felt that the reason for this difference could be looked for in the presence or absence of ganglia. There seemed to be no reason to question the similarity of the muscle in the two different regions of the heart and, as a matter of fact, among the older authors there was no mention of a possibility of such a difference.

Interest in a localization of the motor heart forces was stimulated by the experiments of Stannius. Stannius[28] showed that a ligature placed around the vagus trunk had the same effect as cutting it. If he placed a ligature around the sinus before the opening of the vena cava, the vena cava continued to beat just as that on the other side of the ligature, the latter, however, slower than the veins. When the ligature was placed exactly at the opening, the heart stopped in diastole, whereas the sinus continued to beat. Cutting at the same spot did not always work the same as the ligature. A ligature between the sinus opening and the circular groove caused the portion closer to the ventricle to come to standstill. After ligation of the atrioventricular groove, the ventricle again began to beat. If a ligature was placed around the sinus itself and the auricle separated from the ventricle, the auricle beat synchronously with that of the ligated sinus end. Occasionally remnants of the auricle, which remained attached to the auriculoventricular margin during ligation of the atrioventricular region, remained quiet whereas those combined with the sinus part continued to beat.

Stannius ends his observations with these conclusions: ligation on any spot of the auricle permanently inhibits the beat of that part of the auricle which lies closest to the ventricles as well as the ventricles;

contrariwise, ligation of the ventricular margin incites the ventricle, which before was inactive, again to commence prolonged contraction. He suggests, therefore, the presence of two centers, one an accelerator and one an inhibitor, but believed that the interpretation of this phenomenon was difficult to give.

Bidder[29] set up a difference between rhythmic and reflex centers. Since the former are very numerous we cannot definitely locate them. Nevertheless we must assume that they are in the region of the pulmonary veins. The activity of the reflex centers should be determined. The result of their separation is that a stimulus from a needle prick no longer causes a contraction of the entire heart, but of certain muscle bundles. These centers are to be sought in the atrioventricular ganglia. Automatic function cannot be attributed to them, for after their ablation the rest of the undamaged heart can continue to beat. Since the ventricle still takes part in the pulsation, it is not possible that the conduction of the stimulus from the auricle to the ventricle could take place through these ganglia; it would have to use other hypothetical nerve tracts, if one does not wish to believe that they can be conducted through the net-like union of muscle bundles from one to the other.

Eckhard[30] opposed him. Although he permitted the independent heart beat to be dependent upon the presence of ganglia at the sinus, he observed that the reflex movement of the ventricle can also be noted when it has been deprived of its atrioventricular ganglia. In other respects the mechanism of the reflex movement is not clear, and could possibly be determined through the study of the embryonic heart.

While Eckhard considered the reflex mechanism as questionable, Goltz[31] went so far as to ignore completely the automatic centers and declared that the heart movement was entirely one of reflex action invoked from the blood.

Munk[32] attempted to present a very elegant proof for the reflex nature of the atrioventricular ganglia. By tying off the sinus he brought the ventricle and auricle to a standstill and, by means of a needle prick, produced a single short stimulation. When the stimulation hit the tip of the heart a single contraction resulted; but if the upper rim of the ventricle, which contains the ganglia of Bidder, was touched, the single stimulation produced a series of beats which Munk believed he could explain by the stimulation of the ganglia. The aortic bulb also answered a single stimulation with a series of twitchings.

One should counter that the stimulation hits not the ganglia but the

heart muscle which must transmit its movement to the ganglia with the aid of the nerves, in the same way as the heart tip. At the aortic bulb one often does not find the ganglion cells[33] which Munk postulated. We shall speak later regarding the explanation of Munk's experiments by means of the peculiarity of the muscle at the atrioventricular margin (Gaskell).

Heidenhain[34] interpreted the results of the experiments of Stannius in an entirely different manner from Bidder, Eckhard and Goltz. The ganglia of the heart collectively possess an automatic function, for if one separates the ventricle so that the ganglia of Bidder remain with it, it of course stops at first, but after a time begins to beat; likewise, after ligature of the coronary groove, it does not come to standstill but beats slower. The standstill of the heart resulting from ligature at the sinus margin is to be explained by stimulation of inhibiting nerves lying there. If one counters this with the fact that cutting a nerve produces a stimulation of five minutes' duration, one can state that the vagus is not a simple nerve but contains ganglia, for it is known that disturbance of the vagus nucleus in the oblongata causes long-lasting heart standstill.

A. v. Bezold[35] opposed this. He showed the impossibility of laying the standstill of the sinus segment to vagus stimulation, since this also occurred when the vagus was paralyzed by means of curare. If one assumes a special type of ending of the vagus, which could be found only in the ganglia, these would form the new central inhibiting organ to which Stannius had already referred. Heart movement could be explained only through interaction between accelerating and inhibiting forces. From the investigation it appeared that the former had their seat primarily in the sinus and at the atrioventricular groove, whereas the inhibiting apparatus belonged to the auricular septal wall.

In a similar manner Rosenthal[36] conceived the rhythmic movement as the product of a constant stimulus and a constant opposition in which the latter could be augmented by the vagus. He considered the atrioventricular ganglion as a reserve organ which was inactive normally but which, under unusual demands on the ventricle, could become active.

This concept possessed a peculiar advantage in the simplicity with which the workings of the vagus could be explained; and the symptoms of atropine, muscarine, and nicotine poisoning fitted nicely into this scheme. However, in Haller's words: *dudum experior rarissime eas rerum naturalium interpretationes firmas esse, quae eleganti simplicitate speciem veri imitantur.* (I have for some time realized that those explanations of natural phenomena which seek to imitate the appearance

of truth through elegant means are very rarely trustworthy.) A series of works appeared which stated that the nerves and ganglia of the heart could not form the all-important origin of rhythmic movement as they were considered by Rosenthal, von Bezold and others to do.

Then Engelmann[37] showed that conduction and excitation do not take place through nerves but through transfer from one muscle fiber to the other, in addition to the irritability of the heart.

In 1873 Luciani[38] found that if the heart is tied to a cannula in the region of the auricle and is filled with defibrinated rabbit's blood, it passes over, after an initial increase in frequency, into a characteristic movement pattern in which groups of pulsation alternate with longer pauses. This periodicity could not be of reflex origin and it was impossible to account for the origin of the stimulus for the first beat following the pause.

Likewise, in the laboratory at Leipzig, it was discovered that the ganglion-free tip, mentioned previously, responds to a single stimulation with a single contraction, but could be induced to long-continued beating by filling it with oxygen-containing blood to which can be added numerous other solutions such as delphin, chinin and sodium chloride, etc., which have a similar action. It follows from this that the origin of rhythmic movement does not require the presence of ganglia.

However, there exists this difference between the artificially produced pulsations of the heart tip and the automatic beating of the excised heart: that the former exists only under very special and favorable conditions, that is, the influence of foreign agents.

One was thus forced sharply to differentiate the concept of rhythmicity, that is the capability of answering external stimuli with a series of pulsations, from automaticity, which is the capacity to create within itself the stimuli necessary for movement. It was necessary to ask anew whether the movement of the heart was a pure automatic one or a rhythmic one supported by prolonged stimulation. The objection of Luciani, previously mentioned, was cast aside by the discovery of von Basch that heart muscle was capable of summating single stimuli. Through this one can explain why the heart beat reappears after a pause.

Merunowicz[39] attributed autonomic function to the heart tip because it could be induced to prolonged beating by simply filling it with blood serum, etc. Bernstein[40] objected because such a filling administered an abnormal stimulus to the heart tip. The clamped-off tip of the heart *in situ* remains at a standstill for days, even though it is continually per-

fused with fresh blood; and during this entire time its irritability is preserved. This experiment of Bernstein was substantiated by many. It was determined that if the tip was filled with frog's blood it remained at a standstill, whereas it could be brought into pulsation by a series of chemical, thermic and mechanical (*Druck*) stimulations.

There were divergent points of view regarding the meaning of these results. Since a local relaxation of ventricular muscle (Rossbach) could be produced through slight touching, Aubert[41] believed that the normal condition of the heart muscle was not one of rest, but rather one of change from activity to relaxation; and thus the occurrence of the latter must be considered as a stimulation symptom. In the heart, inhibitory forces and excitatory forces operate on the muscle as well as on the nerves. According to whether one is preponderant over the other, standstill or pulsations occur. In Bernstein's experiment, normal frog blood acted as an inhibiting stimulus.

In contrast to this, Langendorff[42] differentiated true automaticity and pseudo-automaticity, the latter resulting from the penetration of an externally induced stimulus. Like Luciani, Langendorff noticed that following ligature in the region of the auricle there resulted first a very rapid pulse, then standstill, then periodic pulsations, and finally a single pulse which became entirely obliterated. Stimulation during the pause set free the beginning of the single pulse against the end of the group of pulsations. The latter was more easily produced the nearer to the atrioventricular margin stimulation was made. Accordingly, Langendorff considered the atrioventricular ganglia as the automatic centers of the ventricle.

Lucowitz[43] reached similar conclusions regarding the pulse of the heart tip. He, too, saw in it only the action of the stimulus; however, the chemical and mechanical stimulations are not effective in themselves, but only when they penetrate at the same time. Think as you wish about the automaticity of the heart, despite the fact that ganglia are not necessary for rhythmical movement, there was the compulsion to prove anew the influence of ganglia on normal heart movement.

Löwit[44] undertook this problem with greatest care. His results will be very carefully considered, because they set forth most sharply those points which offer the best approach to critique of Stannius' experiments. Löwit emphasized the necessity of repeating the experiments of Stannius with very careful observation of the anatomy of the frog's heart. He

carried out the separation of the heart segments with sharp scissors in order to rule out unavoidable stimulation from ligature. He obtained the following results:

1. In the sinus cut, which leaves the auricle in continuity with the inferior vena cava and part of the sinus, the inferior vena cava beats five to ten beats faster than before; the auricle and ventricle beat somewhat slower.

2. The deep sinus cut separates the auricle and the abutting part of the sinus from the combined vena cava. The inferior vena cava beats slower at first, but then continues in its old tempo; the auricle and ventricle come to a standstill, but after five to ten seconds, begin to beat again. In an atropinized heart the standstill does not occur.

3. The high sinus cut separates the sinus from the auricle and, at the same time, removes a portion of the auricle. This results in a diastolic standstill of the auricle and ventricle. The duration of this standstill varies directly with the size of the auricular piece removed.

4. If the first cut is performed and then a piece is cut from the under side of the auricle, which is in communication with the sinus and is the site of entrance of the septal nerves containing the ganglia of Remak, a standstill of the ventricle and auricle occurs immediately. Ablation of the right auricle may decrease the beat of the ventricle or may leave it unchanged.

5. A cut through the auricle produces a temporary standstill of the heart stump.

6. A cut exactly through the atrioventricular boundary produces slowing of the ventricular rhythm after several beats and finally, if no other stimuli penetrate, it stops.

7. If the cut is made above the atrioventricular margin nearer the auricle, the auricle continues to beat unchanged, whereas the ventricle, after two or three beats, comes to standstill. The standstill results, all the more surely, the farther the cut is removed from the atrioventricular margin. A cut in the tip of the ventricle produces a single lasting contraction in the base.

8. A cut below the atrioventricular margin produces a lasting standstill of the ventricle. The auricle beats on unchanged for a long time, its first pulse after the cut emerging from the ventricular end.

9. If the heart is brought to standstill by means of a sinus cut and then a ventricular cut is made, the effect is the same as in the uninjured heart.

10. If the valve tips are excised from the ventricle after opening it through a long cut, the ventricle stops at once; if only one valve is removed, only the injured side comes to standstill. The ventricle, however, resumes its movement; but it remains in permanent standstill when the piece of the ventricle communicating with the aortic bulb is removed.

Löwit concluded from his experiments that the sinus was not the actual center for automatic heart activity, but rather that the sinus, vena cava, and auricle contained sufficient impulse for contraction within themselves. The main mass of the irritable element lay in the sinus and the auricular septal wall. The ventricle would receive its stimulation, under normal conditions, collectively from the sinus and auricle through

the medium of the valve tips; at least, its contraction is possible when the valve cusps retain their intact relationship with the auricular septum and the ventricular muscle. The concept of an inhibition of the ventricles from the auricle also is not correct. Whether the nerves, ganglia, or the valve muscles do the conducting Löwit left an open question.

In all events, it is certain that the sinus is not the only automatic center, as Bezold insisted, for although through its piece-wise ablation one, to be sure, obtains a slowing of the heart beat, in the meantime this condition is determined by vagus stimulation since it is absent in atropinized hearts.

After Löwit had carried out a number of stimulation experiments showing that heart muscle could be induced to rhythmic movement by constant as well as by intermittent stimuli, he pointed out that, without external stimuli, the auricular muscle, just like the ventricular muscle, would remain at rest. The direct cardiac muscle stimulation experiments carried out by Ludwig's students cannot be the only stimulators of the heart beat. For if one assumes that the combined muscle elements in their totality must work together for regular progressive contraction, then it is strange why ablation of very small muscle masses lying at a very specific point can produce immediate standstill of the remaining muscle elements, whereas one can remove large pieces of muscle in the immediate neighborhood without noticeably altering the heart beat. The concept that the muscle elements which lie at different points in the heart have a different physiological value so that a very definitely circumscribed part is necessary for the release of the contraction of the rest of the muscle elements has little value in itself.

Similar difficulties beset the theory of direct muscle stimulation, in those experiments which cause standstill of the ventricle through the removal of the valve cusps, if one does not wish to assume that the contractions arising from the vena cava and sinus influence the less separated muscle fibers of the valve cusps in order to keep the ventricle in functioning condition.

If the experiments of direct muscle stimulation have established the conditions under which the rhythmic contractions of cardiac muscle are maintained, they do not suffice for explanation of a series of other findings. We are then led again, by exclusion, to the concept that the ganglia of the heart must have an influence on heart movement.

From the hypothesis that the movement-determining stimuli are constantly sent out to the muscle from the ganglion cells lying in the

heart and that, furthermore, the muscle fibers of the heart themselves possess the property of rhythmic contractility which they cannot activate without the aid of stimuli, the results obtained from transection experiments as well as stimulation of the frog heart at once become altogether understandable.

Aubert[45] came to similar conclusions before Löwit's time. He summarized his results in the following words: the ganglion cells and nerves of the heart are not absolutely necessary for the origin of rhythmic heart pulsation, but they are, in the first place, more easily excited and, therewith, a greater guarantee would be given for regulated activity of the heart; they are furthermore necessary to furnish the conduction from the stimulation of sinus to the auricle and from that onto the ventricle; in the third place, the slow conduction through the ganglia, which Marchand[46] found, acts in such a manner that the ventricle is stimulated to beat after the auricle has completed its pulsation, a fact of extreme importance in the regulated propulsion of the blood.

The results which Gaskell[47] obtained were entirely different. He worked partly with the heart of the turtle which offered the advantage, besides its greater longevity, of nerves superficially located and easily accessible. Gaskell differentiates two forms of movement in the heart: spontaneous movement (in our terminology, automatic) and stimulation movement. "The capacity for spontaneous movement decreases with the removal of the sinus." A strip cut from the ganglion-free tip of the heart is hung up and stimulated with an induction current. Contractions arise at the stimulated end which progress along the strip with each succeeding beat; when they reach the other end, the induction stimulation can be omitted; the strip continues to beat spontaneously for 28-29 hours—"stimulation movement."

If the strip is protected from drying and stimulation from the very beginning it begins to beat by itself, after a time—"automatic movement."

If, in the excised but beating heart, the band running along its hinder surface between auricle and ventricle and enclosing the coronary nerves is transected, the ventricle continues to beat synchronously with the auricle; if, on the contrary, without injury to this band, the atrioventricular band was stabbed through, the best progression was immediately and permanently disturbed. If the atrioventricular groove was only partially severed, the progression of the beat was not disturbed; if this bridge is reduced to a certain breadth, only a single contraction of the ventricle occurs for every three or four of the auricle, and so on until

the bridge becomes so narrow that the ventricle beats independently of the auricle. The relation of the number of beats to a certain breadth of bridge was changed by nervous stimulation. More careful observation of the anatomy of the cardiac muscle showed that the sinus, the muscle ring on the margin of the sinus and auricle, as well as the muscle at the atrioventricular margin resemble the embryonic type of cardiac muscle fibers; the bulged-out reticular part of the auricle and ventricle resemble a more highly developed type. The less developed parts retain a higher degree of automaticity. Proof of this is given in the aortic bulb of the ray which consists of embryonic muscle fibers possessing no ganglion cells and which can beat spontaneously with the same frequency as the sinus. Furthermore, the mentioned stimuli are said to be the cause for the hesitation of the contraction wave in the passage from the sinus to the auricle and from this to the ventricle. Gaskell summarizes his concepts in the following statements:[48]

1. The rhythm of the heart is inherent in the muscle tissue itself and not in the presence of peripheral nerve centers.

2. The rhythmic (automatic) strength of each heart part is related, not with the presence of ganglion cells, but with the persistence of the primitive condition of the heart muscle tube.

3. The beat progression rests upon the peristaltic contraction wave which originates in the place possessing the greatest frequency of rhythmic activity; it is slowed down incidentally at the passage of the contraction from one chamber to another as the result of the nature and anatomical arrangements of the muscle tissue at the junction of these parts.

My attention was directed to this work of Gaskell after I had finished my experiments on the chicken embryo and had reached similar conclusions. The agreement of the results greatly surprised me.

The concepts that the sinus was the seat of the highest automaticity; the exclusion of the nerves and ganglia for conduction and coordination of the movement; the significance of the atrioventricular boundary as a remnant of the embryonic ear canal: all agree most beautifully with the concepts derived from embryonic heart activity.

Nevertheless the experiments of Löwit, aided by the findings of Gaskell, did not permit complete interpretation. The continued beat of the auricle and ventricle, after the sinus has been removed except for a small piece at the origin of the auricular septal wall, and the sudden standstill which appears when this small piece is removed cannot be explained from Gaskell's teaching. Careful examination of serial sections of the frog's heart solves this difficulty. The musculature of the sinus is

not in contact with that of the auricle in the entire extent of its boundary. Only at one definitely circumscribed place does an exchange of bundles occur. It is this very place where the auricular septal wall has its origin. Here bundles pass over from the sinus onto the posterior auricular wall and onto the septal wall; with them, of course, the septal nerves course together with Remak's ganglia. In separating this small piece, that part of the sinus becomes ablated which is especially united with the auricle in functional conduction and transmits to it its pulse. Through this the standstill is explainable.

The so-called second part of Stannius' experiment, that is the reappearance of the ventricular pulse by ligation or cutting at the atrioventricular groove, is, as Löwit has mentioned, the result of the stimulus produced by cutting or ligation. It, however, is not dependent upon the atrioventricular ganglia but rather upon the rhythmic, strongly excitable, embryonic type of muscle present in the atrioventricular ring.

If we further point out that, by Fano's experiments on the hearts of chicken embryos, the influence of the ear canals (which as you know are drawn into the basis of the ventricules) manifests itself so that its ablation from the ventricle produces ventricular standstill, and beating can only be restored by warming it, whereas, even though slowed, it kept beating when continuous with the ear canal, an explanation of Löwit's experiments can be made in the following manner:

In the first experiment, the ventricle and auricle were separated from the most automatic part of the sinus musculature. This produced a slight slowing of the heart beat.

In the second case, the slowing of the beat of the vena cava, as well as the brief standstill, is the result of vagus stimulation produced by the cut. This appears from the fact that both conditions are absent in the atropinized heart.

In the third attempt, the main seat of heart automaticity is completely removed from the auricle. It is possible that the immediate standstill may be due to vagus stimulation. After a time, exactly the same as in the transection experiments of Fano and the experiments of Gaskell on the turtle, the automatic pulse of the auricle and of the atrioventricular boundary appears.

In the fourth attempt, the last remnant of the sinus muscle, which up to now was still joined to the auricle, is removed; since the degree of automaticity of the right bowed-out half of the auricle lags behind the sinus, its removal has no influence on the beat rate as long as a remnant of the sinus is still present.

In the fifth experiment, removal of the normal pulse from the sinus results at first in standstill but later gives way to an automatic auricular pulse.

In the sixth attempt, the musculature of the ventricular base and that of the atrioventricular funnel are damaged extensively and stimulated at the same time; therefore a stimulation pulse results with decreasing pulse rate and finally standstill.

In the seventh attempt, removal of the normal stimulation impulse from the ven-

tricle without stimulating the atrioventricular funnel results in standstill. This appears all the surer the farther the cut is made from the atrioventricular rim.

In number eight, separation of the atrioventricular funnel from the heart tip with stimulation of it at the same time results in standstill of the tip of the heart and of the auricular pulse, which originally proceed from the atrioventricular margin.

The ninth case is explained by the foregoing, since the impulse of the sinus is not utilized after stimulation of the atrioventricular margin.

In the tenth attempt Löwit destroyed the atrioventricular stimulus at the same time that he destroyed the valve cusps. He therewith destroyed the union between the auricle and the ventricle either on one or both sides. If the ganglia are carefully removed without damaging the ring (Gaskell), the ventricular beat progression suffers no change. That the ventricle returns to beating, stopping only when the piece of the aortic bulb which is adjacent to the ventricle is removed, rests on the fact that a remnant of the auricular wall and the atrioventricular ring are in closest combination with the base of the bulb. This remnant represents the small curvature of the embryonic heart tube and is easily recognized in frontal cuts of the frog's heart.

Now we may really say that the riddle-like investigations of Stannius, which played such an eventful rôle in the doctrine of heart movement, have been disrobed of their mythical charm and have been explained. We may now rightfully declare as superfluous the concept of motor ganglionic centers in the hearts of cold-blooded animals. We can add also that the hearts of the invertebrates (I refer to the splendid work of Ransom[49]) beat without the aid of motor ganglia. Thus the conclusion appears justifiable that the heart of adult mammals and birds can also get along without them for their rhythmic activity. This is a conclusion which, in consideration of the fact that the embryonic mammalian heart beats in the same form as in the adult even before it possesses any ganglia, could invite a slight criticism of being hypothetical as a concept of motor activity on the part of mammalian ganglion cells; whereas in the cold-blooded animals this same concept has proved itself to be superfluous. Nevertheless, the conclusion could still rest on the probability, and it is all the more pleasing that the investigations of Krehl and Romberg regarding heart movement in mammals have led to exactly the same conclusions. So the question remains to be answered: what is the purpose of the ganglia?

In our first work, Romberg and I expressed the belief that they are sensory organs on which fall the task of transmitting the unconscious sensations arising in the heart to the reflex centers in the cord and brain stem whence the regulation of heart movement, with the aid of the vagus and sympathetics, proceeds.

The following consideration, based upon embryological facts, ex-

presses the same idea. As far as is known, the ganglion cells in vertebrates, which send centrifugal impulses, originate within the region of the medullary groove, from which also arise the central nervous organs. The elements which arise outside of the medullary groove form only centripetal fibers. These are the cells which form the complex of the olfactory ganglia, the sensory head ganglia, the germinal ganglia, and the spinal ganglia. Out of the same ectodermal structures as the above-mentioned cells arise the ganglia of the sympathicus. There is no reason to believe that these make any exception to the general rule.

Undeniable proofs for the motor nature of any of the sympathetic ganglia have not been presented so far. Similarly, an agreement regarding their function has not been obtained. Regarding the question of the relationship of the heart ganglia with the vagus, accelerans, etc., more will be said in another place; discussion can follow on a hypothetical basis until that kind of union is anatomically demonstrated.

The conclusions which can be deduced from the preceding discussion may be summarized in the following statements:

1. The heart of all vertebrates beats at a time when it does not yet contain ganglia.

2. From the very beginning, the single segments of the heart tube of the embryo show marked differences in their physiological characteristics. These are shown in the degree of automaticity and irritability; in their reaction to indifferent and asphyxiating gases; and in their reaction to heart poisons.

3. The movement of the heart in the chicken embryo proceeds from the point of highest automaticity, which determines the frequency of the heart beat. In the uninjured heart this is the venous end of the heart tube.

4. The heart beat in the embryo is originally a peristaltic, progressive contraction wave. The final form of movement appears before the entrance of the ganglia with the formation of trabeculae in the ventricular muscle and the fibrillar structure of the muscle fibers. Thus the characteristics, the planned course of the cardiac cycle, the conduction of the stimulus, and the pause between auricular and ventricular contraction are independent of the nervous elements and are determined by the characteristics of the muscle alone.

5. Heart movement in the adult cold-blooded animal is independent of the ganglia and nerves lying in the heart. In review of the anatomy of the frog's heart one is able satisfactorily to explain the experiments

of Stannius without taking into consideration motor and inhibitory nerve centers.

6. It is possible, with the aid of a probable conclusion, to transfer the results obtained from embryos and cold-blooded animals to the hearts of grown mammals. The correctness of this is supported by the investigations of Krehl and Romberg.

7. The proofs which have been given for the existence of motor and regulatory ganglionic centers in the heart are no longer tenable. The function of the heart ganglia has not been determined with certainty. Their origin very likely indicates a sensory function.

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The Story of the Atrioventricular Bundle with Remarks Concerning Embryonic Heart Activity*

WILHELM HIS, JR.

FORTY years ago a little book appeared entitled "Arbeiten aus der Medizinischen Klinik zu Leipzig."[1] Besides the basic works of Krehl and Romberg, it contained the first account of the atrioventricular bundle and its function. I wish dutifully to make use of my leisure time to go more fully into the story of this work in order to clear up some of its myths and to point to some of the problems which seem to be worthy of investigation today just as at that time.

In 1889, along with Romberg, I became an assistant in the clinic at Leipzig which had just been taken over by Heinrich Curschmann. The first assistant was Ludolph Krehl, who had received his training under E. L. Wagner, Albin Hoffmann, and A. v. Strümpell and still continued a close relationship with Ludwig's institute, where he investigated the structure of the heart according to newer methods.

At that time, following A. Volkmann's lead, the cardiac ganglia were generally considered as the centers for automaticity. Only Engelmann, then at Utrecht, and Gaskell, in Cambridge, repeatedly attempted to show that heart muscle had the capacity of initiating the rhythmic stimuli. But what was the condition in case of disease? Did the weakness of the heart or the pulse anomalies arise from changes due to disease in the heart ganglia or in the heart muscle? Hayem, Birch-Hirschfeld, and Leyden found anatomical changes in the heart muscle of patients with infections. In 1890, Ott in Prague[2] found changes in the heart ganglia of a patient who died in narcosis; and Romberg[3] showed at autopsy an infiltration in both the heart muscle and ganglia of a patient who had been sick with typhus for three weeks.

One day I came along as Krehl and Romberg were discussing these questions. I had just finished an embryological problem under the direction of my father and, knowing the technique, I suggested an embryological investigation to determine if the heart can beat before it contains nerves and ganglia. Romberg agreed and my father placed at our disposal serial sections of human embryos and the photo-micrographic ap-

* Translated by T. H. Bast and Weston D. Gardner, Madison, Wisconsin, from *Klin. Wsch.*, 1933, *12*, 569–574.

paratus of the Department of Anatomy. We built models of embryonic hearts by means of Born's wax plate method and we could show that the ganglion cells of the heart belong to the sympathetic system. Remak had considered them of mesodermal origin; Onody,[4] however, had shown that the sympathetic ganglia arose as buds, as it were, from the spinal ganglia; and my father had shown that they, like these, arose from the neural crest lateral to the medullary tube and reached the body organs by migration.[5]

They belonged, therefore, to the sensory system and, since the physiologists did not know of any nerve to the heart whose stimulation could elicit a beat, we concluded that the heart ganglia too served as the afferent limb of the nervous regulation apparatus. (Langley's beautiful work regarding the sympathetics was just in its infancy at that time.) We presented these findings at the Congress for Internal Medicine in Vienna in 1890. From this it appeared that the heart muscle is also of essential importance in rhythmic function. Krehl and Romberg showed that, also in the warm-blooded animals, the large ganglion complex can be tied off without disturbing the beat progression. Yes, the capability of an increased function was maintained. Krehl mastered the diseased heart in all of its parts and showed the occurrence of local changes. Romberg discovered the significance of vasomotor nerves for circulation weakness during infection.

In the meantime, I investigated the development of the cardiac nervous system in all classes of vertebrates[6] and showed that in all of them the heart beat in an adult manner before it contained cerebrospinal nerves or ganglia.

One thing remained unexplained: the conduction of the stimulus from one heart segment to another. In the embryo the heart consisted of a continuous muscular tube; in the adult warm-blooded animals and, in part, in cold-blooded animals, a connective tissue sheet, which in general forms a complete ring, pushes in between the auricle and the ventricle. It is true that on the upper and under surface of the atrioventricular valves thin sheets of smooth muscle were known. However, their union had not been shown (except by Palladino [see below]). Gaskell[7] had shown that in the frog and turtle the conduction passes through muscle substance. I looked for a muscle bridge in following the serial sections through increasing age stages, finally finding it in adult mammals and also in man. I described it in 1893.

Very few people have read this article. Curschmann (who had risen

in Berlin from a cane doctor to a two-horse-team doctor, who conducted a branch office in Moabit, and then conducted a phenomenal campaign in Hamburg and built the first modern hospital) received the call to Leipzig. His strength lay in the clinical field, but after he had published a physiological work on the semicircular canals he became interested in theoretical work. He was happy that such was continued by his students, he abetted them in every possible way and was greatly desirous of publishing openly the excellent work of the young clinic. This otherwise worldly wise man chose for this purpose a separate publication (the *Arbeiten aus der Medizinischen Klinik zu Leipzig*). The contributions had to be limited and were not permitted to be published elsewhere. Even though a goodly number of complimentary copies were sent out, the distribution was considerably circumscribed and for many years now the volume has belonged to the bibliographical rarities.

It was ten years before the anatomists took cognizance of the A-V bundle. In 1903, Retzer, at the behest of Spalteholz, and Bräuning, at the suggestion of Englemann, tested my results and fully substantiated them. In 1906, under the leadership of Aschoff, the important work of Tawara[8] appeared, in which the hook-up with Purkinje fibers was shown and the bundle was declared as the conduction system. In 1909 this was completed with the discovery of the sinus node.[9] Since then the conduction system has been investigated in every detail and today belongs to the well-known structures of the heart. For its development in man we are indebted to F. P. Mall[10] for a very exhaustive study. Külbs[11] has followed the connection between the A-V bundle and the musculature through the vertebrate series.

Now the priority of its discovery has also been discussed; three names can be mentioned in this connection: Paladino, Gaskell, and Stanley Kent.

In 1876 G. Paladino, professor of histology and general physiology in Naples, investigated the muscle fibers on the surfaces of the atrioventricular valves. These have been known since Reid (1839) and Kürschner (1840) but they have been in part passed over in the textbooks and in part denied for man, horse, donkey, ox, dog, turkey cock, and turtle.[12] Paladino's work was very carefully reviewed in Germany by the anatomists Bardeleben and Boll and the physiologist von Hermann. It is very difficult to obtain, and, among the more recent men, only Retzer has seen it in the original. He has criticized Bardeleben for errors in translation. This review, however, is essentially the same as that of Boll

who lives in Rome, and is like the newer citations to be mentioned. At Berlin I was unable to obtain the original. De Gaetani, however, in his very careful work has transmitted Paladino's findings and, in part, has cited them word for word. I believe, therefore, that one can review the main points of Paladino's work without knowing the original.

According to this, the A-V valves contain: (i) muscle from the ventricle, as extensions of its longitudinal fibres; they lie on the valves and end in them; (ii) a complete continuation of the auricular muscle wall with its longitudinal and cross fibers passing over onto the valves. "The muscular wall of the artery," writes Boll, "does not stop at the annuli fibrocartilaginei of the A-V ostium but extends directly past these into the substance of the A-V valves and finally ends in the following manner: it inserts via a part of the chordae tendineae on the wall of the ventricle itself and in the papillary muscles, thus producing a direct union between the substance of the muscle within the valve and the muscle wall of the ventricle." Bardeleben's review was similar. In 1911 L. de Gaetani, anatomist at Pisa,[13] reinvestigated the observations of Paladino, and, in addition to man and the animals investigated by Paladino, examined the cat, the sheep, and the turkey cock. In a very careful description of the individual animal classes, he reached a similar result—that is, the hook-up of the musculature of the auricle and ventricles over the A-V valves. In man, "fatti anatomici non sono evidenti come nelli altri animali: ("anatomical facts are not evident as in other animals"). The longitudinal auricular sheet projects itself onto the valve, whereas short, flat bundles proceed only a short distance from the ventricle onto the valves.

After the A-V bundle had been substantiated many times and its meaning tested by experiment, Paladino raised the question of priority in 1909.[14] He claimed to have been the first one to show a muscle union between the auricle and ventricle: "che non può eschiudersi che tra i fasci da lui descritti che passano degli atri nei ventricoli vi sia quello cosi detto di His" ("that it cannot be denied that among the bundles described by him extending from the atrium to the ventricle there is this one named after His"); in man, however, one could not speak of a "fascio di His" since, in man, the Purkinje fibers which have been identified with it did not exist. In a similar manner, de Gaetani: "E nessuno dubito che al Paladino va attribuito il merito di avere descritto per primo i fasci unitivi atrioventricolari, e al His quello di avere con esattezza descritto uno di questi fasci, cioè una particolarità di un sistema più complesso il-

lustrato del Paladino." ("And there is no doubt that the tribute and credit goes to Paladino for having first described the bundles uniting the auricle and ventricle, and to His for describing one of these bundles carefully, that is, a particular one of this system which is more completely illustrated by Paladino.")

In the experiments of 1876 in which Paladino observed the valve play in the opened heart, he believed he had recognized that the valve musculature took an active part in the closing of the valves, in that, toward the end of the auricular systole, the contraction was carried over onto the sheet which is tied up with the valve fibers; the valves, thereby, produced an active pull on the papillary muscle. In 1909 he repeated that it is not impossible that a few fibers can go direct from the auricle to the ventricle but "incomparabilmente superiore" the action is on the valves.

De Gaetani, at the end of his very careful work, comes to the conclusion that the accounts which are extant do not suffice to prove the important function of the A-V bundle. According to his microscopical preparations there are histological differences between animals and man. In almost half the latter, the Purkinje fibers are absent for histological union with the myocardium; the sectioning attempts are not proof since the bundle contains numerous nerve fibers.

Paladino had also shown, in his very careful investigation, muscle bridges which tied together the aorta and the papillary muscles via the valves, and de Gaetani has verified this. Paladino had not seen what we call the conduction system today. Both have denied its physiological significance. One cannot count Paladino, therefore, among the discoverers of the conduction system.

Gaskell,[7] who in repeated experiments had sought to prove myogenic automaticity, pointed out that cutting the nerve trunks on the outer surface of the heart in fishes and turtles did not diminish or destroy the beat progression. In 1886 he looked for muscle unions and found them in the frog and turtle, in the form of a ring-like sheet, embryonic in character (large nuclei, narrow crossbands). Cutting this ring destroyed the correspondence between the auricle and ventricle. However, the response was not the same in the entire circuit of the ring; that part of the sheet which lay closest to the nerves and ganglion masses showed this characteristic the least. In this important work it was shown that the conduction of the impulse occurs through the muscle bridges; that these are circumscribed; and that they show a peculiar type of structure. Gaskell's investigations were confined to cold-blooded animals. For these, however,

he made the following statement: The rhythmic capacity of every part of the heart depends not upon the presence of ganglion cells but rather upon the persistence of a primitive condition of the heart muscle.

Stanley Kent[15] started from the problem of conduction and wished to investigate how the continuity of the embryonic heart tube becomes broken in the course of development. In newly born rats, which are born in a peculiarly primitive condition, he found a broad muscle bridge between the auricle and the ventricle, but also in the fully grown rat, "in the case of the junction between the septum ventriculorum and the auricle, the fibrous tissue of the base of the valve penetrates a comparatively short way into the muscle, and, in the deeper parts, the fibres sweep uninterruptedly through from auricle to ventricle. The same state of things may be proved to exist where the right ventricle becomes continuous with the right auricle." In the rabbit Kent found muscle bridges at the septum to the right of the mitral ring and also at the outer side of this ring.

Kent also investigated the guinea pig, hedgehog, cat, dog, and monkey. The higher the animal stands in the developmental series, the less the muscle bridges are developed; in monkeys the fibrous ring is very strong; however there were found, in the entire circut on the A-V margin, scattered muscle bundles which break through the ring and produce a continuity between the auricular and ventricular musculature. Besides that, Kent described spindle- and star-shaped cross-striated cells in the connective tissue of the annulus fibrosus which he considered as muscle fibers and to which he ascribed the capability of conduction.

The anatomical description of the conduction bundle is not very clear, but one can assume from his Figure 3 of Plate 12 that he saw that part of the A-V bundle which passes from the auricle towards the septum ventriculorum. However, he did not follow its course and, besides this, he described not only other direct bridges from the atrial to the ventricular musculature, but also peculiar isolated cells to which he likewise ascribed conduction. These cells could not be found by later investigators like Bräuning and Retzer, and the latter is very likely correct in his belief that Kent had been misled by his staining method, picrocarmine. The other two broad muscle bands which Kent described also could not be found by me or the other investigators. A second publication supports this finding. Both appeared in 1893, in the same year as my observations. Stanley Kent knew as little about these as I knew about his.

II. The Function of the A-V Muscle Union

In 1883 Gaskell worked with the hearts of turtles in which the uniting musculature forms a part of a ring. He cut this ring progressively. Short cuts prolong the A-V interval. With longer cuts the ventricle responds only on the second, third, etc., beat of the auricle; after complete transection of the bridge, it came to a standstill. It began to beat again in its own but slower rhythm, completely independent of that of the auricle.

A similar effect would have to occur in warm-blooded animals by cutting the A-V bundle if it really served as a conducting mechanism. In 1893, aided by Dr. Graupner, at that time assistant to the clinic and later a physician in Dresden, I experimented on rabbits. A reconstruction of serial sections furnished me with information as to the position of the bundle in relation to the septal wall and the A-V valves (Fig. 1).

Under chloroform anaesthesia, the trachea and the vena jugularis were exposed, a tracheal cannula inserted, and tincture of opium and curare solution was injected into the jugular. Then the sternum was cut in half by means of cutting down on a hollow sound; the right and left halves were fastened by slings; the pericardium was split into halves and these likewise fastened laterally so that the heart lay, as it were, on a plate. A clamp was placed at the right heart ear and at the side wall of the left ventricle, and the pulse was registered on a kymograph by means of a thread and a "Marey'sche Trommel."

Now a star knife, whose blade was 10 mm. long and 1.5 mm. broad, was inserted into the tip of the right heart ear and closed off by means of a purse string suture. In that way very few drops of blood were lost. I felt for the septal wall with the tip of the star knife. One can easily distinguish between the flexible auricular septum and the solid, strongly pulsating ventricular septum. A firm thrust was made at the boundary of these, and, after the excitation of the heart elicited by the thrust had passed off, the pulse from both parts was observed and registered. Because of the flexibility of the septum, it was naturally an accident if the narrow A-V bundle was hit. After the end of an attempt, the heart was opened, the position of the cut was indicated in a sketch, and the septal wall removed and cut into serial sections.

In twenty-one attempts the synchronie was preserved eighteen times in spite of extensive injury to the septal wall, in one[8] the arrhythmia ap-

peared immediately; and in a second one, after enlarging the cut, the expected arrhymthmia appeared;[11] in a third it appeared for a short time and then returned to a regular beat. Figure 2 shows the position of the successful and unsuccessful cuts; in attempts 8 and 11 the microscopical investigation showed that the bundle was cut. In the last of these attempts the cut barely grazed the bundle (Figs. 3 and 4). It was proved, therewith, that conduction from the auricle to the ventricle occurs through the A-V bundle.

I reported these results briefly in an article in the *Wiener medizinische Blätter* in 1894[16] and presented them in September 1895, with preparations and curves, before the International Physiological Congress in Bern. I withheld detailed publication for reasons which will be mentioned.

Two physiologists took cognizance of the results: Engelmann, the proponent of myogenic automaticity, and Léon Frédéricq in Lüttich. In 1900 the latter asked me if my detailed publication had appeared: I had to answer this with a no, but gave him my method and several vouchers. L. Frédéricq now worked out a new method. By means of an artificial circulation, he could open the heart without loss of blood and pointed out that, by means of this method, the A-V bundle could be transected.[17] In 1904 his student Humblett carried out this procedure in a dog and obtained arrhythmia.[18] In 1905 he repeated these experiments with a better method, obtaining the same result.[19] Almost simultaneously Hering, using the dog, reached the same conclusion;[20] and Tawara made histological sections of his hearts. In 1905 also Erlanger,[21] who had undertaken the experiments at the suggestion of Osler, recorded the effects of cutting the bundle. (For the chronological sequence of these works see Humblett 1905/6.)

If I now add the experiments of Eppinger and Rothberger,[22] who cut the right and the left bundle separately, the important steps in the early history of the physiology of the bundle are complete.

III. The Adams-Stokes Symptom Complex

That I did not immediately publish a detailed account of a discovery, the meaning of which was completely clear to me, will appear astonishing and unbelievable to those who, in later times, have written a separate article on every one of their experimental attempts. But while I was busy with the transection experiments a patient who suffered from the Adams-Stokes syndrome was brought to my division. At that time this disease

Fig. 1. Relation of the bundle to the aorta and mitral valves, reconstructed from serial sections. Viewed from the left. Rabbit. *Ao* Aorta with semilunar valves. *M* Mitral wing of the aorta. The bundle is indicated in black.

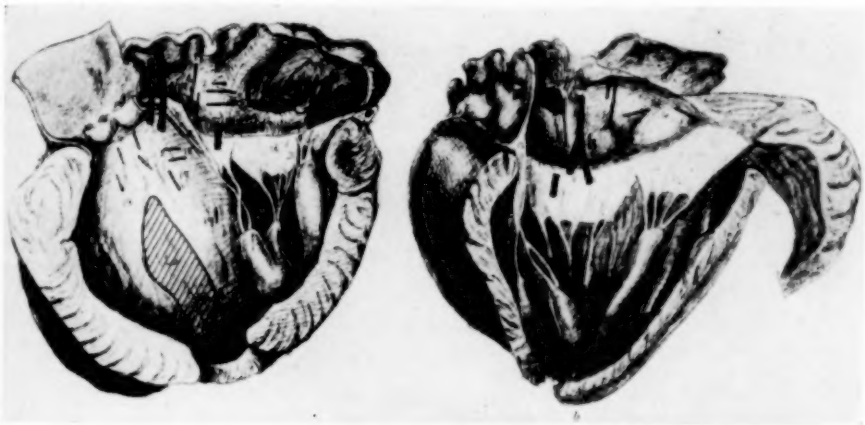

Fig. 2. Summary of all trials. Heart system *a* from left and *b* from right. The effective cuts are indicated in heavy black and the non-effective ones in fine lines.

Fig. 3. Curve from trial VIII. Above auricle, below ventricle, middle time record. At ↑ cut. Before the cut the auricle and ventricle beat synchronously. After the cut the auricle beat 39 times and the ventricle 12 times per 10 seconds.

Fig. 4. Sagittal cut through the heart wall of trial VIII. Atrioventricular bundle in longitudinal view. At ↑ cut, recognized by blood clot. *A* Auricular septum, *B* Ventricular septum.

was not known in Germany under that name, which was given it by Huchard in 1889.[23] Even in the careful studies of Riegel[24] and Grob[25] on bradycardia it was not classified as a separate disease entity. Charcot[26] had seen lasting pulse changes with attacks of unconsciousness, accompanied by unquestionable changes in the medulla oblongata, and therefore considered *"pouls lent permanent"* as a bulbar symptom. Our patient, too, had occasional attacks of unconsciousness and respiratory disturbances without interruption of the radial pulse. At the same time, the sphygmo- and phlebogram showed a complete independence of auricular and ventricular beats, the auricular pulse continuing even during the standstill of the ventricle. Thus the suspicion arose that it might indicate a block resulting from the destruction of the A-V bundle. If this could be shown anatomically, then the circuit would be complete: to anatomy and physiology would be added the pathology of the bundle.

The patient died outside the clinic and it was not possible to obtain an autopsy. Thus, I laid the material aside in the hope of a second case. That hope was never fulfilled, and the increasing number of patients with gout in my section led me into another field of investigation. Not until 1899[27] did I publish my case. Fate decreed that in my long years of clinical activity, I have never had an opportunity to investigate a case of Adams-Stokes syndrome anatomically. Others have been more fortunate in this respect and today this symptom complex is generally attributed to a bundle lesion and it has been investigated in greatest detail.

IV. The embryonic heart

The movable red spot in the germ of the chicken egg which is so formless to the unaided eye fascinated Aristotle, Harvey, and Haller. In 1883 Preyer presented what was known about it at that time in his *Physiology of the Embryo.* Careful experiments on it were first conducted in 1886 by G. Fano,[28] professor of physiology in Florence. He removed the germinal disk from chicken eggs of the second and third incubation days. By means of splitting of the egg membranes to expose the embryo, he made a cut through its back and then, by means of light stretching, gave the closely-folded sigmoid-form of the heart the appearance of a stretched S-shape in which the various segments could easily be differentiated. He recorded their movement photographically. On this object he tested the influence of the temperature, stimulating and asphyxiating gases, electrical stimulation, crushing, and transection. The results are

very noteworthy: he found differences between the venous and arterial ends of the heart tube, so that the automaticity (that is the capability of spontaneous pulsation) and the number of pulse beats at the venous end were the highest; from there they decreased as the arterial end was approached. The excitability, that is the capability of responding to stimuli, reacts in a reverse manner. Every portion of the tube that was isolated by means of a cross cut showed the same polarity. The experiment of Stannius also succeeded in this object. Therewith, the qualitative difference of the heart segments of the embryo was proved to be similar to that found by Gaskell in cold-blooded animals. From the behavior towards oxygen lack and carbon dioxide, Fano concluded that the variations lay in the differences of the wall and, because of this, the difference in the speed of diffusion. Regarding the question of whether the heart at this stage of development contains nerve elements, Fano, in a remarkable manner, responded without a word.

I therefore undertook this study in 1890 after I had determined that the wandering-in of vagus fibers and heart ganglia occurred on the fifth to sixth day. The task was to determine the characteristics of the nerveless heart and to compare it with that which contains nerves, that is to say, to determine when the function of these structures becomes perceptible. With an apparatus which was built according to that of Fano and one that permitted photographic registration, I succeeded in verifying his findings. I enlarged upon them by the use of heart poisons for the testing of which, for example atropine and muscarine, Schmiedeberg had recommended the heart nervous system. Here it was shown that the embryonic heart required unusually high concentrations in order to obtain any reactions; that muscarine did not cause a standstill, and was not an antagonist to atropine; and that a digitalis preparation did not produce a standstill in systole after a pulse slowing but, in a greater percentage of cases, produced standstill in diastole. These results as well as those obtained from stimulation and transection are not altered when, on the fifth and sixth days, the heart receives its nerves. Many of the older hearts could not be investigated by this technique because after the 8th day they are nourished through the coronary circulation and, by destruction of the area vasculosa, are damaged because of lack of blood. The attempts, furthermore, were not satisfactory because the heart during the experiment was noticeably damaged by the draughts and the warmth of the light source (at that time only the lime light was available). One worked on the organ under abnormal circumstances.

In the spring of 1891 I repeated the experiments at the zoological station at Naples on embryos of the sharks Pristiurus and Scyllium. Their hearts reacted towards poisons in a manner similar to the chick, the same when they had nerves and ganglia and when they did not. No changes in characteristics could be noticed after the entrance of the nervous structures. Therefore, I reported only very briefly regarding these observations in my publication of 1893.

In the same year an extensive work by Pickering[29] regarding the embryonic chick heart appeared in London. Pickering observed it *in situ* in the egg; resorted to graphic registration; ignored the damage from preparation and reached, therefore, several anomalous results. He found that the poisons were active in a much smaller concentration than I had found. Digitalinum Schmiedeberg strengthened the systole and finally caused standstill of the ventricle in contraction; muscarine naturally damages only in concentrated solutions through cauterization. His results were: embryonic heart activity is a characteristic of the muscle; the nerves distribute the action of the vagus and sympathicus, their ends being independently subjected to the action of the poisons. In 1896 Pickering[29] extended his work through observations on mammalian embryos, which he observed within the uterus, and through testing of the action of the stream on these as in the older chicken embryos. In older embryos the stream first produces a slowing, and, at the same time, atropine and muscarine acted antagonistically.

Neither these nor Fano's work received sufficient attention; the problem of learning the characteristics of the beating of nerveless hearts did not lure the German physiologists. This conforms to their slight inclination toward comparative physiology with which only Engelmann, Kühne, Biedermann and later Verworn concerned themselves. This one-sidedness was desired because, as Schmiedeberg said to me once, "We have such difficulties in recognizing vital phenomena that we are satisfied to know them only in two or three kinds of animals." English physiologists naturally study the heart only in vertebrates.

It was not until 1909 that again a careful paper on the embryonic heart by A. v. Tschermak[30] appeared. This work on the hearts of fishes (sharks, Petromyzon, Gobius), whose nerve content he investigated histologically, contained his findings that the yet nerveless heart showed basic characteristics like those which are known for the adult heart: refractory period, compensatory pause, maximal reaction, and universal stimulus conduction. In contrast to this, it was shown that sensitivity to

artificial stimuli was relatively small, the refractory period surprisingly long, and the behavior towards poisons similar but not the same. Tschermak concluded from this that the four basic conditions in the heart muscle are independent of the nervous system; this latter, however, besides the regulatory function of these characteristics, modifies them neurotonically. The normal function of the heart, according to this, would represent the manifestation of a myogenic capacity in a special neurogenic-determined condition.

In 1913 Külbs,[31] at that time assistant in my clinic, began to record the movements of the embryonic heart kinematographically and electrocardiographically. In the latter, Wertheim-Salomonsen had preceded him. Külbs, with the help of Cremers, improved the method and could determine that, on the third incubation day, the electrocardiogram agreed in all essential points with that of the adult. He could show conduction disturbance through lesions at the A-V margin; in older embryos the isolated right and left bundles were successfully destroyed, which Eppinger and Rothberger had found in the adult. Külbs could continue these attempts until the tenth incubation day. The entrance of the nerves and ganglia produced no change in the electrocardiogram. This work was interrupted in 1914 and could not appear until 1920.

I have attempted the production of nerveless hearts by destroying the neural crest in the frog, and was able to produce a larva without a vagus, but I was not able to keep it alive. Hooker[32] was successful in doing this with a special technique, in 1910. In 1911, Burrow[33] prepared embryonic heart cultures and was able to keep them beating for generations. Finally, Philip Stöhr, Junior[34] taught how to explant heart anlages to any part of the body desired.

Here the important works on the characteristics of the embryonic heart are exhausted. For a period of forty years, they are not too numerous in the face of the vast series of observations on the adult warm- and cold-blooded hearts. Among most of the physiologists they have received surprisingly little attention. I know of no summarizing piece of work and, even in the most extensive summaries of heart activity, they are dealt with in a very casual manner. I confess that I have never rightly understood this reluctance of the physiologists. Their argument has always been: that which beats is not yet a heart muscle but an embryonic cell of a different structure. That was emphasized when the attempt was made to carry over the characteristics of the embryonic beating heart to the adult. Even Haberlandt,[35] an adherent of myogenic automaticity,

warns against the transposition of these characteristics; and Bethe,[36] in a very detailed discussion, expresses the view that the myogenic nature of the heart beat of the chick embryo is not proved, for at the time the heart begins to beat it still consists of undifferentiated cells and not of muscle fibers; also, in explantations, the activity preceded the fibrils (Olivo[37]). Asher[38] bases his position on the rule of v. Uexküll: the embryonic condition is differentiated from the succeeding condition by a critical point which stipulates a profound functional difference; and furthermore the development of the structure goes along with the inhibition of the function. Tissue cultures and explants retain the embryonic character.

That can be admitted, but two things are overlooked. The organs of digestion, metabolism, excretion, and respiration are not needed by the embryo. They can differentiate in peace. Its heart becomes functional almost immediately after the tube has closed. This, however, is not a mere rhythmic movement, but the anatomically yet undifferentiated tube has all of the qualities which are referable to the adult heart: automaticity and irritability, polar arrangement of these, latency, compensatory pause, the all-or-none law, every form of rhythmical disturbance, Bowditch's steps, Luciani's periods, and electrocardiogram. Only in the behavior towards poisons and in the degree of its irritability are there a few differences. That a morphologically yet unfinished tissue possesses already all of the later characteristics is in itself a biological problem of great interest and it is no less interesting to follow its changes in the course of its differentiation.

If one assumes, with the proponents of neurogenic automaticity, that these characteristics at a later time are conveyed by the nervous elements, then it certainly would be a gripping biological problem how one tissue could take over the function of a second. There was a time when the disputed question, neurogenic or myogenic, was fought over with a dogmatic zeal. Thus von Kronecker, even though he was a personal friend, never wanted to let any of my arguments bear any weight. Even more severe was von Cyon (who described the depressor nerve from Ludwig's laboratory and who led a double existence as investigator and as agent of his government in Paris) who could not refrain, even in his article on world opinion, from speaking out against the evil myogenic adherents.

Since then the discussion has become quieter, and one can say that through the investigation of embryos, the knowledge of the muscular conduction system, tissue cultures and explants, the adherents of the

neurogenic automaticity have been pushed back more and more into a defensive position. They rest on the basis that all remaining rhythmically-moving hollow organs are nervously stimulated and also that nerve fibrils are present in all parts of the heart. One could add thereto still a second argument. We believe to have shown that the young embryos are free from ganglia and nerves from the fact that these nervous structures wander to the periphery from the neural crest and out of the spinal cord. Now Stöhr Junior[39] tends, like Remak in his time, to consider the origin of the ganglion cells from the peripheral mesenchyme. This is not proven, and even less, whether and how that kind of primitive structure could function; but at the same time, that kind of possibility cannot be cast aside *a priori,* but for tissue cultures and explants it naturally plays no rôle.

It is possible that the question of autonomy may win an entirely different appearance when it becomes established that it is determined hormonally as Otto Loewi, Haberlandt, and Demoor believed that they could show. But in this case the separation of muscular and nervous function must support itself on the studies of the nerveless heart tissues. The technique is given in part and is capable of being developed in part during the time of the micro-manipulators and magnifying apparatuses. Much valuable material is at hand. What is lacking, however, is a study of it from all possible angles. Experience teaches us that investigations which are based upon one object or on only one method can easily lead to wrong impressions and are subject to criticism. The knowledge of the nerveless beating heart, and the meaning of the nerve function derived therefrom remain today, as was the case forty years ago, a stimulating and promising but incompletely solved problem. To call attention to this fact is the purpose of these lines.

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Notes and Queries

Edited by RALPH H. MAJOR, M.D.*

History of Pharmacy in Holland

The history of pharmacy has had some prominent representatives in Holland. During the last decades they were mostly Pieter van der Wielen, Professor of Pharmacy at the University of Amsterdam, and Henryk Cohen, "Privaat Docent" (comparable to the American assistant professor) of the History of Pharmacy at the University of Leiden, who had worked successfully in the field. Professor van der Wielen died in 1947, and Dr. Cohen passed away in a concentration camp during the occupation of Holland by the Nazis. Since the death of the latter there has been no academic teaching of the History of Pharmacy in Holland.

Fortunately, this gap has now been closed in a most promising way. Dr. D. A. Wittop Koning, owner of a pharmacy at Amsterdam who during the last decade has proven his knowledge and ability in a number of historico-pharmaceutical publications, has been appointed "Privaat Docent" of the History of Pharmacy at the University of Amsterdam and started teaching on March 23, 1949.

In addition to numerous articles, Dr. Wittop Koning has published two books concerning the early and the more recent history of pharmacy in Holland.

1. *De Handel in Geneesmiddelen te Amsterdam tot Omstreeks 1637* (Purmerend, 1942). This book of 136 pages, the author's doctoral thesis, offers far more than its title intimates. The reader is given an excellent report on the trade in drugs from the thirteenth century until about 1637 based on documentary evidence and listing not only the kind and amounts of the drugs concerned but also the prices. Furthermore, the book illumines the relations between the apothecaries and the "kruideniers," the wholesalers and, often simultaneously, retailers in herbs, shedding new light on the origin and development of these groups and touching on the history of the respective guilds.

2. *De Nederlandsche Maatschappij ter Bevordering der Pharmacie 1842-1942. Benevens Overzicht der Nederlandsche Pharmaceutische Tijdschrift—van 1755 tot Heden.* This volume of 251 pages represents in fact two books bound together: a history of the "Royal Dutch Association for the Advancement of

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Pharmacy" and a "Survey of the Dutch Pharmaceutical Journals from 1755 until Today."

The history of the association throughout the first century of its existence (1842–1942) covers everything to be expected in such a compilation of data and is by its very nature factual rather than entertaining. It is enlivened by a series of portraits.

The "Survey of the Dutch Pharmaceutical Journals" will attract more attention because this part of professional history has in general not been made the subject of thorough research and presentation. Dr. Wittop Koning has done an excellent job. The study, well illustrated with portraits of editors and reproductions of title-pages, gives in all brevity a clear picture of the development in Dutch pharmaceutical journalism. The title might be somewhat misleading. The "Tijdschriften" appearing between 1755 and 1785 can hardly be regarded as "pharmaceutical" in the sense of having been devoted exclusively or even mainly to pharmacy. Not only were they very ephemeral, but they tried to cover the whole field of "geneeskunde," *i.e.*, medicine, with pharmacy as a part of it.

The "Chemische Oefeningen voor de Beminnaars der Scheikunde in het Algemeen, en de Apothekers, Fabriekanten en Trafiekanten in het Bijonder," issued from 1785 to 1788, was a commercial undertaking trying to serve a number of special groups, among them pharmacists. The same holds true for the "Chemische en Physische Oefeningen . . .," appearing from 1782 to 1798. Hence it seems to be justified to consider the "Schei-En Artsenijmengkundige Bibliotheek," issued from 1824 to 1834 and edited by B. Meylink, "apotheker te Deventer," not only as the first Dutch pharmaceutical journal under the editorship of a pharmacist (as Wittop Koning says), but as the first really pharmaceutical journal to appear in Holland.

According to personal communications, Dr. Wittop Koning has succeeded in creating a standing committee on the history of pharmacy in the Dutch pharmaceutical association. Among his plans is the continuation of Stoeder's *History of Dutch Pharmacy* (1892). Referring to an essay of this writer entitled "Historical Research in Pharmacy" (*Amer. J. pharm. Educ.*, 1946, *10*, 271–285). Dr. Wittop Koning challenged the statement that "the European situation being entirely clouded and offering not much prospect for decades to come, we have to restrict ourselves to the situation within the United States."

This writer gladly admits that recent European publications in the field have proven him to be wrong. He is looking forward with much confidence to the fulfillment of Dr. Wittop Koning's "hope to show that this statement . . . is a little bit too dark."

As a matter of fact, in this case nobody could be more happy of a rebuke than the present writer.

Madison, Wisconsin GEORGE URDANG

François Poupart

Of those who are acquainted with the structure known as the inguinal ligament, or crural arcade, there are comparatively few who know anything of the life of François Poupart, whose name has become associated with it; and of these still fewer may have read the account of his finding the structure. François Poupart was born at Le Mans on March 3, 1661, and was educated at the monastery there, where he soon became interested in the works of Descartes and the study of nature. After spending many years in this fashion he decided to embark on a medical career and, as Le Mans offered no facilities for this, he went to Paris. At first, as a means of subsistence (for his parents were by no means wealthy), he undertook the care of a child, but finding that this left him too little time for his own studies, he gave it up and devoted himself entirely to his books and lived a life of extreme frugality. He made a special study of insects and possessed the patience and skill to make the most delicate dissections. In order to perfect himself in the study of anatomy, he applied and was accepted for the post of Surgeon at the Hôtel Dieu and, though he had had no previous experience in this, he astonished everyone by his prowess. Three years later he gained the degree of Doctor of Medicine of the University of Rheims and in 1699 was admitted to the Académie des Sciences as the pupil of Jean Mery, chief surgeon of the Hôtel Dieu. His interests were not confined to the subjects already mentioned, however, but he was also considered an able student both of geometry and of architecture. Most of his writings deal with the structure, life and habitat of insects, and perhaps the most noteworthy of these papers are the one on the leech and the one giving the correct account of the insect popularly known as the "Cuckoo-spit" (*Histoire de l'Académie Royale des Sciences,* 1705). Towards the end of October, 1709, he fell ill and died within a few days.

The account of the inguinal ligament is to be found in the *Histoire de l'Académie Royale des Sciences,* Paris, 1705, p. 51 and is as follows:

> M. Poupart a parlé de deux gros Ligaments ronds, fort visibles, puisque dans les grandes personnes ils sont longs de plus d'un demi-pied, et dont cependant les Anatomistes n'ont point traité, apparemment parce-qu'ils n'en ont pas connu les usages. Ils sont attachés par un bout sur la crête de l'Os des Iles, par l'autre bout sur la crête de l'os Pubis et le milieu porte à faux. Ils font la fonction d'os en cet endroit, car ils soutiennent les trois grands Muscles de l'Abdomen, c'est à dire, l'Oblique externe, l'Oblique interne, et le Transverse. Leurs fibres tendineuses à peu près paralleles entre-elles vont s'attacher à ces Ligaments. Ils sont situées immédiatement au dessous des Anneaux.
>
> La pensée de M. Poupart est qu'ils peuvent soutenir et rompre en partie l'impulsion que de grandes roux, des sauts violents, etc., donnent aux Intestins, et par là les empêcher de s'insinuer entre les Anneaux, et de former des Hernies. De plus ces Ligaments tenant lieu d'os, quelques Os que la Nature eut mis à leur place, le Ventre en auroit eu moins de liberté de s'étendre, sur tout dans les grossesses. Par ces raisons, M. Poupart appelle ces deux Ligaments "Suspenseurs de l'Abdomen."

Royal College of Surgeons of England JESSIE DOBSON

The Birth of Transfusion

The report from Paris a few years ago of the death of Dr. Alexis Carrel brought to mind a story of that eminent scientist which, after nearly half a century, may now be accepted as medical history.

It was the writer's privilege, two score years ago, while serving as a Fellow of the Rockefeller Institute for Medical Research in New York, to share an apartment on the upper west side of the city with three other members of the staff. One of these was the young French research surgeon, Dr. Alexis Carrel.

Dr. Carrel at that time was carrying on his experiments in the transplantation of organs, especially the kidneys from one dog to another, a piece of work for which, three years later, he won the Nobel prize. The secret of his success was that he had developed a technique by which he could sew arteries and veins, leading to and from the kidneys, together end-to-end without causing clotting of the blood, so that the circulation to the transplanted organs could be maintained and their life and function continued.

One Sunday morning in the year 1908, while the other three of us were lolling in the sitting room of our apartment and wondering why "Alec" was sleeping so late, he came into the room, sat down on the couch and said in his precise clipped English with its strong French accent:

"Boys, I had a most interesting experience last night and want to tell you about it. Did you hear some people in the sitting room during the night?" When we told him that we had, he said that his visitors were the three Doctors Blank, naming three brothers who, in that day, stood at the very top of the medical profession in New York City, an internist, a surgeon, and an ophthalmologist. After introducing themselves they told Dr. Carrel that the ophthalmologist's wife had given birth to a baby three days before. The infant was bleeding to death from hemorrhagia neonatorum. Would Dr. Carrel please try to transfuse some blood from a healthy person into the baby in an effort to stop the bleeding and save the infant's life—a procedure which, up to that time, had never been accomplished.

To this request Dr. Carrel demurred by saying, "Alors, how can I do that? I have no license to practise surgery on human beings in the State of New York. My patients are only my dogs and my cats."

The surgeon then said: "But do you not understand, Dr. Carrel, that this is a question of saving the life of my brother's child? You are the only man in the world with the technical skill to perform the operation we desire. It is your experience in anastomosing the tiny blood vessels of your dogs and cats which makes us believe that you, and you alone of all living surgeons, can do a similar operation on the three-day-old baby. As far as the legal side of the question goes I will act as your assistant to the best of my ability. Technically I will be the operator, you my assistant. This will take care of the legal aspects of the case."

With this assurance Dr. Carrel agreed to make the attempt, though he was more than dubious of the outcome. He went to the Rockefeller Institute, got the tiny instruments with which he operated on his animals and accompanied the three physicians to the home of the ophthalmologist.

The account of the operation can best be given in Dr. Carrel's own words as he told it to us on that Sunday morning. Though forty years have passed since we listened to the tale, the story was so dramatic that I think it can be retold almost verbatim.

"I went to the house with the three doctors. Here the sight that met my eyes was pitiful indeed. The young mother was lying on her bed, still weak from her confinement and terribly worried over the condition of her little babe. The baby was beside her, as white as the sheet on which it lay, apparently almost bloodless and quite unconscious. I feared that it would die before I could prepare for the operation.

"When I asked who wished to give his blood, a real quarrel ensued. I was deeply impressed with the difference in the viewpoint of you Americans from that of my own French. I love my France, but I know that if a similar situation had arisen in France there would also have been a quarrel, each person expostulating that one of the others should be the donor and enlarging on the reasons why he himself should be excused. Here, too, there was a quarrel. But in this case the disagreement arose from the father, the mother and the two uncles each insisting that he was the proper one to give his blood. As they could not agree, the matter was left to me, and I decided in favor of the father.

"The father and the baby were placed side by side on a table. The father's wrist was bound firmly to the baby's leg. The radial artery of the father and the popliteal vein of the baby were dissected out, cut and, after being well impregnated with vaseline to prevent clotting of the blood, were sewed together end to end. The operation was quite simple, as the vessels were much larger than the little renal vessels of my dogs and cats on which I am used to working.

"While the baby at first was so weak from loss of blood that it did not stir or cry when I dissected out the vein, in a few moments after the anastomosis was completed and the father's blood was entering the vein, it began to move. Soon it was whimpering and a faint pink color appeared in its cheeks. It was not many minutes before it was red all over and crying lustily. I then tied off the father's artery and the baby's vein, cut them apart, sewed up the wounds in the skin, accepted the parents' profound thanks and came home to bed. It was a most interesting experience."

The baby lived; its bleeding stopped; the collateral circulation kept up the nutrition of the father's hand; and the first attempt in the history of the world at direct transfusion of human blood was a brilliant success.

Utica, New York T. WOOD CLARKE

A Ten-Year Index for "Ciba Symposia"

Readers of the *Journal* are no doubt acquainted with *Ciba Symposia,* a periodical devoted to the historical and cultural aspects of medicine and its allied fields, which has been published since 1939 by Ciba Pharmaceutical Products, Inc., Summit, New Jersey. This periodical has been issued primarily in the interest of the medical profession but has been found useful and of interest by non-medical readers. As 1949 marks the tenth year of its publication, the material that has appeared in *Ciba Symposia,* Volumes I to X inclusive, is now being indexed for the benefit of readers who have kept complete files. The *Index* will comprise three sections—names, illustrations and subjects. It probably will be ready by September 1949, and will be sent on request. Those who wish to receive the *Index* should write to Sales Service Division, Ciba Pharmaceutical Products, Inc., Summit, New Jersey.

The Ciba Collection of Medical Illustrations

When the medical history of our time comes to be written, it will not be possible to discuss the medical education of the practising physician without taking account of the various educational materials published by pharmaceutical manufacturing concerns. One of the most significant of these publications has just appeared under the title, *The Ciba Collection of Medical Illustrations.* This book embodies plates that had previously been issued as portfolios of anatomy and pathology from 1940 to 1948. These pictures, the work of Frank H. Netter, M.D., have now been bound in one volume (9½ x 12½, 224 pages) and are being sold at the cost of printing as a service to physicians and medical students. All inquiries should be addressed to Department 500, Ciba Pharmaceutical Products, Inc., Summit, New Jersey.

GEORGE ROSEN

Medical History in Foreign Periodicals

From time to time, as such items come to our attention, we shall bring to the notice of readers of the *Journal* historical articles appearing in foreign periodicals.

BRAZIL

Pedro Nava: Capitulos da Historia da Medicina no Brasil (Chapters in the History of Brazilian Medicine). *Brasil Médico-Cirúrgico,* 1948, *10,* 181–238; 399–414; 517–548.

Revista de Medicina do Rio Grande do Sul, Sept.–Oct. 1948, *5* (25), is devoted to various aspects of the history of medicine in Rio Grande do Sul, Brazil.

CHINA

The Chinese Journal of Medical History, October 1948, *2* (*3* and *4*), is a special number presented to Dr. Yü Yun-Hsiu on the occasion of his seventieth birthday, October 28, 1948. It contains the following papers:

H. C. Fan: A Study of the Character "I"

C. K. Tsang: Supplement to the Pentsao Kangmu

Sung Hsiang-yuen: Medicine and Taoism in the Eastern Han Dynasty

Yeh Ching-chiu: Yeh Tien-shih Discards Chai Hu for Malaria

C. M. Ting: Postscript to the Nanking Pentsao Kangmu

D. G. Lai: Medico-historical Gleanings

T. Y. Sung: A Short History of Ancient Literature Upon Intestinal Parasites in China

Y. Ch. Lieou: A Historical Note on Babinski's Sign

Hsieh Tang: Terrenz's Structure of the Human Body

Chien Pang-hsien: The Medical Profession in the Four Histories.

These papers are all in Chinese but have English abstracts. One article appears in English:

B. E. Read: The Identity of Chiao Yao

GERMANY

Friedrich-Wilhelm Bayer: Bemerkungen zur gegenwärtigen Lage der deutschen Medizingeschichte (Remarks on the present state of medical history in Germany). *Grenzgebiete der Medizin,* 1948, *1,* 245–247.

Walter Artelt: Vom genius loci in der Medizingeschichte (On the *genius loci* in medical history). *Grenzgebiete der Medizin,* 1948, *1,* 248–249.

Johannes Steudel: Brunschwig's Anatomie. *Grenzgebiete der Medizin,* 1948, *1,* 249–250.

ITALY

Giuseppe Pezzi: Medici navali del '700 (Naval physicians of the 18th century). *Annali di Medicina Navale e Coloniale,* 1947, *52,* 427–447.

Giuseppe Pezzi: Terapia medica delle ferite da arma da fuoco nel '600 (Medical therapy of gunshot wounds in the 17th century). *Annali di Medicina Navale e Coloniale,* 1948, *53,* 124–132.

Rivista di Storia delle Scienze Mediche e Naturali, January–June 1948, *36* (1) contains the following papers:

Benedetto Biagi: Il famoso processo a carico del grande scienziato Lazzaro Spallanzani (The famous trial of the great scientist Lazzaro Spallanzani), pp. 3–20.

Mariano Cipriani: Contributo allo studio etimologico del vocabolo "Sifilide" (Contributions to the etymology of the term "Syphilis"), pp. 21–37.

Mario Battistini: Medici Italiani nel Belgio nella prima metà del secolo XIX (Italian physicians in Belgium in the first half of the 19th century), pp. 38–54.

Alcide Garosi: Pagine di storia della medicina Senese (Pages from the medical history of Siena), pp. 55–64.

Francesco Giugni: Carlotta Buonaparte e il tragico destino dei Napoleonidi (Carlotta Buonaparte and the tragic destiny of the Buonapartes), pp. 65–71.

Andrea Corsini: Pietro Betti (Da alcuni documenti inediti) (Pietro Betti. Some unpublished documents), pp. 72–92.

TURKEY

Zeki Başar: Türk Tip Tarihi ve Tarihte Tibbiyeli (Turkish medical history and the medical student in history), *Sağlik Dergisi,* 1948, *22,* 385–400.

GEORGE ROSEN

History of Science Society Meeting

The 1949 meeting of the History of Science Society will be held in conjunction with the annual meeting of the American Historical Association at Boston late in December. Plans are now being made for the program, and members of the Society interested in submitting papers for consideration should communicate with the Chairman of the Program Committee, Professor Henry E. Guerlac, Cornell University, Ithaca, New York. No papers can be considered after October 1, 1949.

National Congress of the History of Medicine

The fifth Congresso Nazionale della Società Ital. di Storia delle Scienze Mediche e Naturali is being held in Milano on 2–3–4 October 1949. The general theme of the Congress will be "Medicine of the Renaissance."

Book Reviews

I. Reichborn-Kjennerud. *Vår gamle Trolldomsmedisin* [Our ancient Magic Medicine]. Studies published by the Norwegian Academy of Science. Oslo, Jacob Dybwad, 1928–1947. 5 vols. (Vol. I, 1928, 284 pp.; Vol. II, 1933, 212 pp.; Vol. III, 1940, 221 pp.; Vol. IV, 1944, 263 pp.; Vol. V, 1947, 253 pp.)*

Dr. Reichborn-Kjennerud came well prepared to his self-imposed task. Even in Norway where a working knowledge of the major languages is taken for granted among scholars, he is considered a linguist. His feeling at home in various idioms, ancient and modern, as well as a keen historical sense, helped him to throw much light on the formation of medical vocabulary. Norway has no chair in the history of medicine, but in the midst of a busy professional life he has sustained an unflagging interest in this subject and is at present preparing a supplement to the above volumes on the subject of death and immortality in magic medicine. Numerous papers have passed from his desk to European and American periodicals. He has been and is an enthusiastic counselor to other workers in his beloved field as indicated by the following excerpt from the Introduction to *An Old Icelandic Medical Miscellany* (Oslo, 1931) by the American scholar Henning Larsen:

> The problems of medical, botanical and pharmacological history, dangerous enough to the expert, presented many a pitfall. If these have been escaped to any degree it is largely due to the indefatigable interest of Dr. I. Reichborn-Kjennerud . . . who read the whole work in proof and in numerous letters presented suggestions, corrections and additions. . . . Evidence of the extent of his contribution will be found throughout the volume, where his initials constitute one of the most frequently met symbols.

When the anniversaries of men and institutions are celebrated it is often said: What a pity that someone has not collected and set down in writing the traditions and stories connected with them! This Reichborn-Kjennerud has done for the history of magic in the north as well as for the whole world, for on many of the outermost skerries, in the shut-in mountain valleys, pre-historic legends have survived which are the property of all peoples although often in different forms. According to archeology, Norway has been inhabited for the past ten thousand years, but the history of the Norwegian state extends back only to the end of

* Each volume forms a complete unit with footnotes for each page listed immediately following the text, bibliography not given in the preceding volume or volumes, and an index. In Volumes III-V, in addition to the bibliography of printed works, there is a list of communications from various sections of Norway containing information requested in letters sent out in 1911 by F. G. Gade and Fredrik Grön. These communications are now preserved in the collection of Norwegian folklore in Oslo. In Volume V, in addition to footnotes, bibliography, and subject index for all five volumes, there is a list of Old Norse words occurring throughout the text. An indication of the tremendous amount of work involved may be gained by observing the number of pages devoted to references in Volume I alone: footnotes, pp. 214–260; bibliography, pp. 261–273; index, pp. 274–284.

the ninth century, at which time Iceland was colonized largely by people from the west coast of Norway. In Iceland a remarkable school of history and literature developed in the eleventh and twelfth centuries; the many sagas written in eighteenth century style make fascinating reading today.

With the coming of Christianity to the north (*ca.* 1000) new weapons were acquired for the fight against evil spirits causing disease: holy water, saints and their bones and blessed wells, the Virgin Mary and Holy Scripture. On the other hand Satan, the great deluder, was added to the side of evil. Leech books did not come to the north until the latter part of the thirteenth century but many of their recipes had reached Scandinavia long before that through the folklore grapevine. Apothecaries' shops came late to the north compared with the southern countries. Denmark came first; drugstores are mentioned there around 1456. None of the men and women who practised medicine in the early days has left written records.

Between the first chapter of Dr. Reichborn-Kjennerud's book, dealing with primitive medicine, and the last, discussing alcoholism in the north, the author has assembled "all the ills that flesh is heir to" and some of the spirit as well. In giving the different manners of treatment he points out that there is little difference between popular medicine and that of the schools in the early days. Surgery here as elsewhere was in a class by itself, being the result of the practical experience of generations. Of special interest are the chapters on epidemics, including that of the Black Death whose imprints still exist in place names and legends, diseases of nutrition such as rickets and scurvy, skin diseases, toothache, insanity, epilepsy, and alcoholism. That there is some overlapping is inevitable and expected.

While, as indicated earlier, magic has existed since the beginning of time when sorcerers or medicine men constituted the only professional class, and while the same superstitions or beliefs turn up in different parts of the world, they often wear a different aspect. Among the many queer remedies found in Galen's drug shop on the Forum was fat, that of the lion being considered the most potent. In the north, bishops' fat was considered the most effective and was handed over the counter as such, being probably lard. Odin, the chief patron of the healing art in the north in heathen times, carried the head of Mime with him for divinatory purposes, much as the South Sea Islanders asked advice from shrunken and decorated human skulls. On the other hand, ghosts were as disagreeable in the north as elsewhere, and from Iceland to Greece patched walls of homes testified to temporary openings having been made for the removal of corpses so that the ghosts would be unable to find their way back. In the early days, with the more healthy be-damned-to-you spirit of the vikings, man killed clean, like a dog. It is sad to have to relate that the north later fell in line with the rest of Europe in the torture of epileptics—who heretofore had been protected by law—and insane people as witches. Both Calvin and Luther believed in witches.

While witch hunts fell off in the south of Europe (*vide* Colbert's edict of 1682 in France), they gained in the north, raging in Scandinavia throughout the greater part of the seventeenth century. In 1669 there was a truly terrible outbreak in Dalecarlia, Sweden. The last case of torture and death recorded in Sweden was in 1723.

In the section on alcoholism the author discusses its well-known hold upon the north, and shows that this had to some extent a religious and magic origin. In antiquity, beer was considered holy in that it received its strength from the earth, a strength capable of counteracting all evil. Even down to our time it has often been customary to pour some beer on the roots of certain trees and on the field where grain for the brewing had been harvested—"what the earth has given, it wants returned." In the same way an Italian gardener will leave some peaches on the ground at harvest time "to return them to the tree." Although the distilled liquors did not reach the north until the late Middle Ages, a reputation as heavy drinkers early became attached to the northmen. As above mentioned, much of this may be traced back to the ancient religious aspect of beer drinking and brewing. Reichborn-Kjennerud cites the testimony of a pastor in Telemark toward the end of the seventeenth century: "The farmers here are very devout when they are brewing beer for a festival for fear that otherwise it will not be potent enough. When the party is in progress and someone is discovered who is not a little-how-come-ye-so they feel that the curse of God is upon the person of whom it is said: 'God help the one on whom His gifts have no effect.' If it happens that the guests at a festival remain sober, the host goes about as sad and solemn as if his barn had burned down. Therefore many will simulate drunkenness even when sober so as to comfort the host and show him that they are not accursed." An often recurring incantation asks for the ability to drink all day long without becoming senseless.

Properly arranging the material from ancient and modern sources—from Scandinavian as well as European records put down before history was written in the north, from the Elder Edda which in point of language belongs to the period 500–1200 A.D., from leech books and traditions by word of mouth—the author has in these five volumes built up a significant epic, a wealth of source material for poets, novelists, and historians, as well as a fascinating storybook for everyone. Like Herodotus he has related the stories as he found them, leaving to the reader to muse on man's long and tremendously painful struggle to conquer death and disease. While the author evidently enjoyed himself enormously writing the first volumes, it must have been a solace to him to keep faith with the past during the years of the German occupation when he wrote the last volumes of this monumental work, tracing the association of magic and medicine in their development down the ages.

Jersey City, New Jersey ANNE TJOMSLAND

GEORGE SEAVER. *Albert Schweitzer*. The Man and His Mind. New York and London, Harper and Brothers, 1947. xiii + 346 pp. Illustrated. $3.75.

CHARLES R. JOY AND MELVIN ARNOLD. *The Africa of Albert Schweitzer*. With a concluding essay by Albert Schweitzer. New York, Harper and Brothers; Boston, The Beacon Press, 1948. No pagination. Illustrated. $3.75.

PHILOSOPHER, theologian, musician, author and above all a practising Christian, Albert Schweitzer was of mature years when he took upon himself the task of going to Africa as a physician to the Negro. In 1905, he suddenly decided to become a medical missionary in French Equatorial Africa. The suddenness of this decision was more apparent than real, however, for it was actually the fruition of many years of development, and grew out of Schweitzer's reflections on his own right to happiness.

When he arrived at this decision, Schweitzer was *privat-dozent* at the University of Strassburg, and had gained distinction as an organist in Paris and Barcelona. Now he began to study medicine at Strassburg, and was occupied until 1912 when he received his medical degree. At the same time, his wife qualified as a nurse. The following year Schweitzer set out for Lambarene in French Equatorial Africa. In 1917, he and his wife were interned in France, and the work that had been carried on for four years was interrupted until 1924. It was during this period that he brought to completion and published his two-volume work on the philosophy of Western culture. Today he can look back on more than three decades of work at Lambarene, for in 1949 he enters his probable retirement after thirty-six years there.

The two volumes under review present an excellent picture of the man, his work and thought. Mr. Seaver gives an admirable presentation of Schweitzer's ideas and his accomplishments in the fields of philosophy, theology and history, and provides a framework for these in the story of the outward events of Schweitzer's life.

An excellent supplement to the biography is the striking picture-and-text "documentary" volume by Joy and Arnold. Here we have a vivid pictorial record of Schweitzer's work at the forest hospital at Lambarene. The jungle backdrop, patients and their relatives, the hospital workers, mothers and babies—all these appear and with them everywhere the rugged figure of the old doctor, that great personality of our time, Albert Schweitzer.

GEORGE ROSEN

SIR ARTHUR KEITH. *Evolution and Ethics*. New York, G. P. Putnam, 1947. 246 pp. $3.00.

THIS thoughtful, vigorous set of essays is a contribution by a scientist of great distinction to the problem which has been agitating mankind since the promulgation of the theory of evolution—the relationship between human traits which

have been valuable in the "struggle for survival" and the good society. Sir Arthur Keith's position resembles that of Thomas Huxley, in his Romanes lecture of fifty years ago, in which Huxley pictures man's nature, as it had manifested itself throughout the evolution of *homo sapiens,* as being essentially evil and intractable, held in check by an ethic which is not rooted in that nature. However, he takes an even more extreme view than Huxley in recognizing human civilization as part of Nature. Keith bases his argument on the degree to which anti-social traits, such as a strong belligerent loyalty to the in-group, have been useful in maintaining small group solidarity, but appear as obstacles in man's attempt to build a world embracing a social ethic. The whole argument is of greater interest when placed in a historical context, the same historical context which is dramatized in the recent publication of *Touchstone for Ethics,* which places T. H. Huxley and Julian Huxley's Romanes lectures in juxtaposition. If Keith's argument is pursued rigorously, it can be equally well argued that traits which are useful in the survival of individual men, in competition with other individual men, would have presented an insurmountable barrier to the establishment of small tribal groups. He lists no trait, in his list of anti-social but evolutionarily valuable traits, for which this argument cannot also be advanced. But, if traits once useful to the individual have been so socialized as to become useful to the tribe, there then remains no valid reason why they cannot be socialized as to be useful in larger and larger group contexts. The whole argument poses an essentially false question as to whether habits of enmity and amity are more innate and valuable.

The book is valuable as the record of a serious and responsible mind grappling with the implications of evolutionary theory in a nineteenth century climate of opinion, still committed to the idea of original sin, however secularized. Modern anthropological and psychological studies now make it possible to do what Julian Huxley has done, and graft the development of a social ethic firmly into the life history of the developing human individual, and so consider it part of the evolutionary process. It is no longer necessary to accept the nineteenth century counsel of despair, that evil had a biological basis opposed to the higher values of civilization, which must somehow be conjured up out of nowhere, without aid or comfort from man's original nature. Interested students of the history of thought in this field will find it revealing to reread Darwin's *Origin of Species,* and realize what different weight would be given today to the two conflicting themes of struggle for survival and the co-operative possibilities of diversification.

American Museum of Natural History MARGARET MEAD

JOSIAH COX RUSSELL. *British Medieval Population.* Albuquerque, University of New Mexico Press, 1948. xvi + 389 pp. $6.00.

POPULATION is one of the most publicized biological factors implicated in histori-

cal causation. To a very considerable degree this interest derives from the work of Malthus, which in a modified form still shapes public opinion. Even though the original Malthusian formulation implied that population change was a result rather than a cause, an inert rather than a dynamic factor in history, writers such as Benjamin Franklin and others took the view that the demographic situation can be a dynamic force in history rather than merely an inert one. Franklin pointed out that "cities do not, by natural generation, supply themselves with inhabitants; their deaths are more than their births," thus implying that increasing urbanization of an area would tend to restrict the growth of population in that area.

In general, the use of the population factor for explanatory purposes in historical analysis has been dominated by interest in a particular contemporary problem. In the nineteenth century this was a fear of overpopulation and population pressure, and even today, when the character of the problem in Europe and America has changed, this type of thinking may still have a historical influence as an ideology, as witness the German cry for *Lebensraum*.

While historians have attempted to explain certain historical changes, such as the decline of Rome, as essentially demographic phenomena, few historical studies of population have been undertaken. Beloch's work on ancient and medieval populations is a notable exception. It is therefore all the more welcome to have this study of British medieval population by J. C. Russell. England is strategically important for the historical study of population because of the splendid collections of archival material. Among the records of the past are four great collections that bear upon demography. These are the Domesday Book, a survey of landholders in 1086; the extents, later surveys of landholders; inquisitions post mortem, documents that often contain data about deaths, ages and heirs; and the poll tax returns of 1377, including the population of fourteen years of age and over. In addition there are certain lesser sources.

The author has taken full advantage of these materials, and has made a splendid contribution to this phase of historical study. After considering the problem of the evidence, which is essentially that of the validity of the numerical data, he analyzes each of the four major sources mentioned above as to the nature of the material and the types of data to be found in each. Succeeding chapters then deal with birth factors, length and expectation of life, factors of mortality, trends of gross population and distribution of population.

While Russell does not emerge with any final conclusions, the effect of population on historical change seems to be that demographic change results from other, more deep-seated elements, and that demographic influence favors certain phases in a culture at the expense of others. The actual direction of the historical process is determined by other factors. This may be illustrated, for example, by the relations between economic crisis, demographic decline, and disease in fourteenth century England. From the studies by Russell in the volume under review,

as well as from earlier writings of Lipson, Dobb and others it would seem that population declined after 1300, probably due to declining productivity of labor on the peasants' lands. The immediate effect of this development was to threaten feudal society with a shrinkage of revenue and to produce an economic crisis. Thus the interests of the landholders were brought into sharp conflict with those of the agricultural laborers. To this situation was added the destructive effect of the Black Death, which intensified the demographic decline and the economic crisis. From this it would seem that the traditional account of the effect of the Black Death on the social and economic structure of medieval society, and with it the theory of the significance of disease as a factor of change in human history requires revision.

This study of British medieval population is difficult to summarize because of the detailed information which it contains. It is an invaluable reference work for all who are interested in the history of population, in the history of medicine, or in the history of medieval Europe.

GEORGE ROSEN

W. H. S. JONES. *The Medical Writings of Anonymus Londinensis.* Cambridge, The University Press, 1947. viii + 168 pp. 12s. 6d.

THE work on Greek medicine here first translated into English seems to be of unusual interest but mediocre value—a paradox that holds true of many scientific treatises produced in the ancient world. Since the work is recorded on a papyrus written around 150 A.D., it carries us back at a stroke over some eighteen centuries of shifting and uncertain manuscript and printed tradition, and since it also discusses Hippocrates at some length, its discovery and announcement aroused a hope that here might be found a solution to the vexed "Hippocrates question." It was in the *Classical Review* for 1892 that Frederic G. Kenyon first described the find and printed a number of extracts. The following spring Hermann Diels, eminent Berlin authority on early Greek philosophy and science, traveled to the British Museum, spent his Easter holidays examining the papyrus, and, "assisted by Sir F. Kenyon and unexpectedly clear weather in London," prepared an excellent edition of the text. This appeared in 1893 in the Berlin Academy's *Supplementum Aristotelicum,* III, 1, and is reprinted by Jones with almost no change. In the same year Diels published in *Hermes* a discussion of the literary and historical implications of the work. From this it was evident that the London Papyrus 137, far from solving the Hippocrates question, added new perplexities; also that the historical section—the middle of the three parts into which the work falls—is no masterpiece. In his introduction the English translator even speaks of it as "this scrappy fragment, with its disappointing summary of Hippocratic doctrine." Even so the papyrus as a whole is of great interest to historians.

In approximately two centuries since the rise of modern historical criticism, several questions of eminent literary authorship—notably the Hippocratic, the Homeric, and the Pauline—have been raised, and the discussions of all of them have passed through strikingly similar stages. In the first place, among the materials traditionally assigned to the author—72 documents in the case of Hippocrates—some were found so discordant from the others in subject matter and style that a common authorship seemed impossible. Then, by a painstaking, systematic sorting, the documents or episodes of the traditional corpus were separated into a genuine core and a spurious fringe. As this analysis, necessarily to a large extent subjective, gathered momentum, more and more of the materials fell under suspicion, until inevitably some extremist arose to declare the whole literary ascription fictitious. Presently, against radical conclusions of this type, common sense reasserted itself, producing such sad witticisms as the remark: "The *Iliad* and *Odyssey* are, of course, not by Homer but by another man of the same name." Finally, after a generation or two of debate and repeated examination of the evidence, a sort of compromise solution was more or less agreed on, with these two principles clearly implied:

First, that literary criticism is never an exact science, but can at best produce only varying degrees of probability.

Second, that practically any ancient writing or body of writings, if handed down by manuscript transmission, has had a more complicated literary history than we at this distance can reconstruct in detail.

This mature stage of criticism—a blend of courage and caution, of credence and questioning—is well represented in the introduction to the work under review, and certainly the two principles have seldom been better illustrated than in the criticism of Papyrus 137. The salient points in its analysis are as follows.

The main work is all in the hand of a single scribe, though an official rescript and a medical recipe in a slightly less cultivated hand have been added on the back of the papyrus. Was the main work copied by a professional scribe or by some physician or medical student for his own use? Pretty clearly the latter.

The text falls into three distinct parts: (1) a set of definitions of medical terms; (2) a résumé of the different theories regarding the cause of disease, as held by twenty Greek medical authorities, seven of them otherwise unrecorded, Hippocrates (460–375? B.C.) being the earliest known, and none being definitely datable after 300 B.C.; (3) a sketch of the medico-physiological theories of several authorities after 300 B.C., discussing especially the οἰκονομία—a sort of bookkeeper's balance—between the intake of the body (through in-breathing, eating of food, and absorption through visible or invisible pores) and its output (through out-breathing, excrement, and emanations from the pores). Did these come to the scribe as three separate documents to be copied in succession, or as one document in three sections or chapters? The latter seems a shade more probable.

The presentation, taken in the large, has a logical arrangement such as teach-

ers in all ages have liked to use in their lectures or textbooks: first, definitions of technical terms; next, an historical survey of the subject; then, a theoretical discussion of current problems. In details, however, the style of the work is careless, choppy, occasionally self-contradictory, and generally immature. Are these, then, the notes taken by a pupil from the oral presentation of a master, or are they excerpts made directly from written sources by a non-literary medical man for his own use? Either hypothesis would meet the facts, but the theory of lecture-notes is the more favored of the two.

And what can be said as to the previous written sources? There must have been some, used either by the supposed teacher in preparing his lectures or by a compiler in making his excerpts. One source is fairly certain. The earliest history of Greek medicine of which we have record was the work of Menon, who was assigned by his master Aristotle to cover this field, much as Theophrastus was assigned to cover natural history. Galen (131–201 A.D.) knew this medical survey, which he says was commonly spoken of as Aristotle's though admitted to be basically Menon's. It has since perished. By reason of its date it could not have brought the subject down beyond about 325 B.C. Now, the middle section of Papyrus 137 cites no recognizable medical authority later than 300 B.C., and for several whom it does cite, among them Hippocrates, it professes to report what Aristotle has said about them. "Aristotle" is here almost certainly the lost Menon. Does the historical section of the papyrus correspond to the Menon-Aristotle history of early medicine in anything like completeness? Obviously not. Some parts of the section quote directly from the author under discussion at the moment. When, for example, Menecrates comes up for consitleration (p. 77), explicit reference is made to his book, *Medicine*. Actually, Jones would like to believe that the lecturer (compiler?) used "not Menon's work, but an imperfect *précis* of it," yet he admits that such an hypothesis is "probable but unprovable."

The third section of the text is a wide-ranging but highly technical discussion of the pores and of absorption through and emanation from them. Many aspects of digestion and breathing are also involved. The pores include not merely those of the outer skin but also "pores visible by reason" in the walls of the veins, arteries, heart, lungs, gullet, stomach, intestines. Modern science would class many of the illustrative examples under the term osmosis, as when the finer parts of food and drink are said to pass through the walls of the digestive tract to nourish other organs, or when some of the inhaled air enters the blood and passes from the veins or arteries out into the body. The general background for such a discussion is unmistakably the medical school of Methodism, which held that most diseases were caused by a blocking of the pores at some point or other in the body. The school was represented at Rome early in the first century B.C. by Asclepiades, and a little later by his pupil, Alexander Philalethes. Both of these are repeatedly quoted in the papyrus, and their theories and others that come up for discussion are not only criticized but often ridiculed unsparingly. For ex-

ample, in one argument the followers of Erasistratus are said to "show themselves poor scientists" (p. 107); a certain reasoning of the Empirics is declared "very foolish and misleading" (p. 121); and it is said of an observation of Asclepiades: "But the man is ridiculous" (p. 141).

Here, obviously, is no historical survey, but a lively debate on current problems. The section sounds for all the world like a lecture—or rather perhaps a course of lectures—delivered in the uninhibited mood of the German professor who took up another professor's book with the remark: "Dieses dumme Buch von meinem Herrn Kollege." Max Wellmann in 1922 (*Hermes,* LVII, 396–429) concluded that this vigorous, authoritative manner, coupled with the Eclectic-Methodistic subject matter, and reinforced by a somewhat obscure reference in a certain passage of Galen, all pointed to Soranus, the most eminent of second century Methodists, as the author of the section. As to this theory of authorship the comment of Jones is noteworthy: "So with some hesitation the Soranus-hypothesis may be accepted as a provisional theory until it can be definitely disproved, or is replaced by one with more extrinsic and intrinsic probability." From so seasoned a critic this may be reckoned an expression of enthusiasm.

All of these facts, probabilities, and unanswerable questions, along with hundreds of lesser points, are set forth in the introduction and may be tested out by any interested reader in the English translation. Without necessary recourse to the Greek text he will sense, from even a cursory reading, the unmistakable atmosphere of the lecture room, the complete intellectual freedom prevailing, and the keen observation and close reasoning employed. He will, of course, learn no medicine applicable today. If the Hippocrates question intrigues him, he will be interested to read the half-dozen pages on the medical beliefs of a man by that name (pp. 35–43). From only a little comparison of this passage with the generally accepted works of the Father of Medicine, he will see why Diels believes it to be based on Menon's misapprehension of a certain document, while Wellmann believes the passage to concern a wholly different person, namely, Hippocrates, the son of Thessalus, grandson of the great Hippocrates. The author of the papyrus text, after an unhappy struggle over the preposterous beliefs ascribed by Aristotle (Menon) to the Coan, concludes grumblingly: "Yet it must be said that what Aristotle tells us about him does not tally with Hippocrates' own statements about the origin of diseases" (p. 43). Manifestly, the Hippocrates question is already being raised—and not answered—near the beginning of our era.

The translation into English is a triumph over almost insuperable difficulties, caused partly by the mutilations in the text and partly by the lack of specific English words to match the medical terms of the Greeks. Having translated the works of the Hippocratic Corpus for the Loeb series, Jones was the natural choice for this new task. His version presents the sense of the emended text faithfully, in smooth and idiomatic English. In fact, he probably gives to the work a higher literary polish than it had in the original Greek. (Line 7 on page 117 contains

an accidental slip, a curious reproduction of the Greek custom of using a singular verb with a neuter plural subject.)

The general reader will be especially interested in the last 18 pages, containing supplementary chapters on "The Nature of Greek Thought" and "The Nature of Greek Medicine." These stress both the help and the hindrance which medicine has had from the different aspects of Greek philosophy. Its complete freedom, unresting curiosity, and disinterested love of knowledge for its own sake were assets. Its fondness for sweeping generalizations and artistically constructed systems, largely unchecked by the appeal to utility or to experiment, was a liability. The philosophers developed the laws of logic, and cultivated in particular that most exact of the exact sciences, geometry. But since there are in nature no perfect circles or straight lines, and since logic proves an inadequate guide to the conduct of men, animals, or atoms, the Greek philosophers undoubtedly hampered medicine, and natural science generally, insofar as they imposed on it their own type of thinking. This conflict between the speculative and the sicentific spirit is by no means new but is here expounded with exceptional clearness.

The latest chapter in the conflict is not mentioned, though so keen a scholar as Jones cannot be unaware of it. Within the last fifty years serious doubts have arisen as to whether any natural sciences are really exact, except as the limitations of the human mind compel them to be so. We can really follow only one line of thought at a time, and our mentality is designed to function best on the human level, where without special apparatus we can recognize both the manifold diversities and the many approximate uniformities in human character and conduct. The social studies are therefore inexact sciences, and we can make them assume the aspect of exactness only by concentrating for the moment on the similarities, let us say, of all Republicans, or all left-handed batters, or all pneumonia cases, and neglecting their differences—in other words, by using the statistical method. By such means we can bring social phenomena little by little within our range of observation and comprehension. The biological sciences, on the other hand, are semi-exact, apparently not because individual differences are there lacking, but because we have little interest in the personal peculiarities of ants or microbes and are not equipped to observe them without microscopic or other assistance. We usually treat them statistically because that method satisfies our purposes. And now the last half century has raised more than a suspicion that chemistry and physics, which long were regarded as extremely exact sciences, are inherently no more exact than any others. Atoms and even electrons are shrewdly suspected to have individual differences, though our powers of observation are not suited to detect them. Down on this level all our science is "statistical" from sheer necessity.

If such reasoning is correct—and at best it is based on analogy—then the most exact science in the world is, with respect to its correspondence to nature,

the most inexact. The Greek philosophers did not, as they themselves supposed, cultivate geometry so assiduously because it best represented reality. They cultivated it because it offered ideas simple enough for the human mind to comprehend. To this day, by our controlled experiments in which we try to allow only one factor to vary, we try to invest our sciences at least momentarily with a similar simplicity. The world, we have concluded, is not limited by logic, circles, and straight lines, but we know that our own thinking largely is.

Army Medical Library, Cleveland Branch WILLIAM JEROME WILSON

OLAF LARSELL. *The Doctor in Oregon. A Medical History.* Portland, Oregon, Binfords and Mort, 1947. xvi + 671 pp. Illustrated. $10.00.

GOOD local history is one of the most effective contributions that medical historians can make to an understanding of medical development. Indeed, one may go further and say that the intensive study of local history is absolutely essential to this end, for without it primary data of importance may be lost.

Realization of this viewpoint is gradually gaining recognition in the United States, and several excellent state histories are now available. Outstanding among these is Blanton's *Medicine in Virginia.* Alongside it, however, I believe we may now place Larsell's one-volume medical history of Oregon. Beginning with the earliest doctors who came to the Pacific Northwest with the explorers and fur traders, Dr. Larsell follows the activities of medical men in this area, not only as practitioners of the healing art, but also in the economic and cultural development of the state of Oregon. The development of medical education, medical societies, legislation relating to medical practice, the care of mental patients and of the tuberculous, the establishment of hospitals, and an account of major outbreaks of communicable disease are all considered in this compendious volume. Special attention is given to women physicians, and homeopathic physicians.

One may hope that in time we shall have medical histories for every state (not unlike the English county histories) which will provide the historian with material for over-all studies in the medical history of the United States. For the present, we must remain satisfied with such splendid contributions as Blanton's *Virginia,* Nixon's *Texas,* and Larsell's *Doctor in Oregon.*

GEORGE ROSEN

The Autobiography of Benjamin Rush. Edited with Introduction and Notes by George W. Corner. Published for The American Philosophical Society by Princeton University Press, 1948. 399 pp. Illustrated. $6.00.

BENJAMIN RUSH—physician, reformer and revolutionary patriot—is one of the most interesting figures in the early history of the United States. A graduate of

the College of New Jersey and a house pupil of Dr. John Redman, Rush went abroad in 1766, and graduated at Edinburgh in 1768. In the summer of 1769 he returned to Philadelphia, and in August of the same year was appointed professor of chemistry in the Medical School of the College of Philadelphia, the first medical school in the American colonies.

Rush actively espoused the cause of American Independence, served in the Continental Congress, and signed the Declaration of Independence. In addition, as soon as war against the British government broke out, Rush volunteered to serve in the field, and was accepted. In his capacity as military surgeon, he saw action on the battlefield, and also wrote a practical manual of hygiene for the Continental Army which was published in 1778 by order of the Congress. From 1799 until his death (1813), Benjamin Rush was Treasurer of the United States Mint.

As a doctor, he was a transitional figure making keen observations on the one hand, and, on the other, erecting and imposing logical medical systems based on few data. Actually he was one of the last leaders of a medicine that had not yet completely freed itself of medieval tradition.

In the summer of 1800 Rush began to write his autobiography for his own private satisfaction and for the edification of his family. Writing in such spare time as he could find, he set forth in ten small notebooks the story of his travels through life. It was not until 1905, however, that part of this material was printed in a volume privately published by Louis Alexander Biddle, a descendant of Benjamin Rush. In addition to the autobiography, Rush also kept a commonplace book from 1792 to 1813.

The text of the autobiography, together with the commonplace book have now been published without deletion under the editorship of Dr. George W. Corner. This edition is an excellent work of scholarship. Dr. Corner has edited the volume with painstaking care, and has added notes of great value for an understanding of the text. In addition, he prefaces the text with a useful introduction. There are also a chronology of the principal events in Rush's life, four appendices, and an index. The binding and typography are handsome and provide a fitting physical setting for this important historical source. Anyone interested in American history, medical history, or simply in an interesting human being is urged to read *The Autobiography of Benjamin Rush.*

GEORGE ROSEN

MAJOR GREENWOOD. *Some British Pioneers of Social Medicine.* London, Geoffrey Cumberlege, Oxford University Press, 1948. 118 pp. $4.00.

BECAUSE he "simply must praise the men who loved doing little sums" (p. 109) and because the munificence of the Heath Clark Trustees exposed "a garrulous

man to temptation" (Preface) we now have for our delectation a precious short book giving the emended and extended texts of Major Greenwood's lectures, delivered at the London School of Hygiene and Tropical Medicine, in 1946. The lectures are, in the main, devoted to the praise of Chadwick, Farr, and Simon. Thrown in are thumb-nail sketches of John Graunt, William Petty, John Howard, John Coakley Lettsom, Thomas Percival, John Ferriar, and Southwood Smith. Florence Nightingale, Karl Pearson, and Francis Galton appear, to no disadvantage, at the tail end of the procession "of those who loved doing little sums."

The professor emeritus of epidemiology and vital statistics is naturally expected to write with a bias toward his competences; and Greenwood does so. But in addition he indulges in many delightful asides (or are they in the main stream) on Virgil's poetry, on medical education, and on the comparative span of the gulf between the best informed 5 per cent and the public, in 1796 and in 1946. On this score he opines, and we concur, that "the gulf between the best informed 5 per cent in 1946 and the public is greater than in 1796" (p. 18).

It is a pity that the author, as stated in the Preface, denied himself the opportunity freely granted him to air his views "on modern social-medical legislation, the planning of research, or even the disastrous consequences of not reading Virgil." The chips of this master's work shop are as precious as, and more intelligible to the common man, than his *works*. (*Vide* pp. 74 and 75 for a mélange of "asymptotic values," "backward extrapolations," and "the empirical formula $A.e^{B(1+r+r^2+r^3+\ldots r^{y-1})}$".)

Major Greenwood's *obiter dicta* are pregnant and provocative while his biographical sketches, even though engagingly charming in style and emphasis, are after all but "tales retold." Such criticism as this were presumptuous if it were construed to reflect on the author's rights to tell what tales he chooses. The intention is rather more to praise the dicta, than to disparage the biographies. In witness stand the Epilogue, and Appendices I and II of the work. Appendix II is particularly noteworthy, for therein Greenwood touches on a subject in the exposition of which he is singularly felicitous. The subject—epidemic constitution—comes closer to social medicine than any other part of the text.

The title of Greenwood's book, as already noted, is *Some British Pioneers of Social Medicine*. But the subjects and substance of the book are little related to social medicine. They rather relate to humanitarianism, environmental sanitation, public health, and vital statistics. To represent Chadwick, Farr, and Southwood Smith as pioneers in *social medicine* is really unwarranted and confusing. They were pioneers in public health, in sanitation, in vital statistics. They could and they have been called pioneers in government medicine. But they were not, and may not be considered to have been, pioneers in social medicine, unless this term is intended to be the equivalent, a sort of modernized synonym, of public

health. *And that is precisely the sense in which Greenwood employs the term.* In the Introduction, the author's definition of social medicine is given "once and for all" as "those applications of medical and scientific knowledge to the prevention and relief of suffering and to the raising of a standard of living which could only be effected by social agencies, by co-operation." The telling portion of this definition lies in the qualifying phrase "only be effected by social agencies." This qualification, *i.e.,* beyond the competence of the individual to perform or to achieve *for himself,* has been the touchstone of public health. Those matters concerning and affecting the health of the individual which the individual cannot attain for and by himself are the proper concern and responsibility of public health. This has been and is the stock argument for the extension of public health into the spheres of diagnosis and therapy. "The individual cannot attain this for himself: the state must do it for him." Hence the common proposal that the national health insurance programme be placed under the supervision of the Surgeon General of the United States Public Health.

In naming those of his fond predecessors who "loved doing little sums" as pioneers of social medicine, Greenwood succumbs to a widespread error. For to many concerned with the subject, social medicine is but preventive medicine wedded to the social sciences. It is preventive medicine, illuminated and expanded by the economics of production and distribution, by the science of housing and city (town) planning, by industrial efficiency and sanitation, by mental hygiene, by the arts and science of recreation in the order of the Peckham Center, by day nurseries, efficient, communal housekeeping, and so on. Now, if such be indeed the nature of social medicine, then Chadwick for certain, and the others by an act of generosity, could be brought forward as precursors of John Ryle.

But the facts are that the union of preventive medicine, i.e., public health, with the social sciences does not yield social medicine, but only government medicine. This was witnessed at the time of Chadwick in the legislating of sanitary laws, and in our own times in the origin and spread of socialized, more properly to be called governmental, medicine.

The crux of the matter is just this: nothing added to the prevailing clinical medicine, nor to the prevailing public health, or preventive medicine, can yield social medicine. For the basic theoretical, or conceptual foundation of current clinical medicine, from which public health and preventive medicine derive, is in direct opposition to the conceptual foundation of social medicine. The science or *technos* of clinical science can be incorporated into social medicine, but the reverse is not possible. It is not feasible to expand the argument, at this time and in these connections; but to indicate the lines along which it could be developed, it may be pointed out that clinical medicine always begins with and is properly concerned with specific pathology, specific ætiology, and specific therapy. It approaches the individual from without inward. Social medicine follows

the opposite approach, and is concerned with what has been and is the inimical complex of forces of which the individual's overt disorder is but an easily perceptible witness. Specific pathology, specific ætiology, and specific therapy are, in the conceptual data of social medicine, but fixed instances in a dynamic process vastly wider and vastly deeper than, taken by themselves, they, i.e. specific pathology and specific ætiology, can reveal.

The Polish wife of an American husband, he sick (peptic ulcer) and unemployed, and she pregnant, undernourished, and anæmic, purchased breakfast cereals at 18 cents the pound, but would not use the canned juices provided free of cost by the relief agency, nor cook up whole wheat grain with raisins (brown sugar and evaporated milk to be added), even though it was shown to her that this combination was less costly and more nutritious. The war period offering employment to wife and husband, both went to work, and with the first money gained they purchased a pony cart for the oldest daughter, aged 12, a console radio, and a second hand car.

Curative medicine cannot remedy the ills of this all-too-typical family. Social medicine might at least save their children.

Despite all this, Major Greenwood's brief book is a delight to read and is salted with that wise humanism that has always been characteristic of his writings.

New York Academy of Medicine IAGO GALDSTON

RENÉ SAND. *Vers la médecine sociale*. Paris, J.-B. Baillière et Fils; Liege, Editions Desoer, 1948. 671 pp. (no price given).

JOHN A. RYLE. *The Natural History of Disease*. Second edition. London, New York, Toronto, Oxford University Press, 1948. xiv + 484 pp. $3.75.

A. E. CLARK-KENNEDY. *Medicine*. Vol. I, *The Patient and His Disease*. Baltimore, Williams and Wilkins Company, 1947. xii + 383 pp. $5.00.

RECENTLY the term social medicine has gained wide currency. The rapidity with which this has taken place is striking indeed, so that the meaning of this development is a matter of some import. Is social medicine just a new name popularized by a passing fad? Is it the expression of a fundamentally new idea unknown to the past? Or does it represent an awareness of a need for reformulation in our day of an older purpose which had been allowed to drop out of sight with the passage of time, and for the implementation of that idea in the light of the best medical knowledge of the present? Answers to these questions may be found by reviewing the origin and tracing the development of the concept of social medicine.

For some forty years René Sand, Professor of Social Medicine at Brussels,

has been developing a broadly-conceived and vital approach to the social relations of health and disease. In the present volume Dr. Sand traces historically the various strands that have contributed to the growing fabric that will be the social medicine of tomorrow. The book is divided into nine major sections dealing with the history of the medical profession, hospitals, individual hygiene, social hygiene, occupational medicine, public assistance, the social sciences, and the future of social medicine.

Vers la médecine sociale is based upon an extensive knowledge of the relevant literature and thus provides an invaluable work of reference in this field. But while the warp and the woof are of good quality, the fabric has not been well woven. Without causation, generalization, synthesis, it is not possible to write history. We are more interested in the processes into which things enter than in things as such, in a web of interconnection rather than in discrete entities, in the significance of facts relative to connections and not in facts or statements about them as absolute in themselves. Thus, while Dr. Sand quotes numerous statements of nineteenth century French authors attesting to their recognition of the fact that in large measure social factors are basic in the causation of disease, especially mass disease, nowhere is there any indication that philosophically this idea derived in part from Cabanis' specific physiological development of Condillac's sensualism, and that it was taken up by Saint-Simon and transmitted to a number of medical men. Or, that these and related ideas developed in France were transmitted to England and Germany and helped to provide the ideological underpinning for the activities of Virchow, Neumann, Farr, and their contemporaries. In other words, from the point of view of historical method the fatal defect of Dr. Sand's volume is that it does not undertake a genetic analysis of its subject and is consequently unable to present an adequate historical synthesis. This kind of history of social medicine is still to be written.

Nevertheless, this is one of the most important contributions to social medicine to appear within recent years. Exceedingly significant are the last thirty pages where Sand discusses the definition and characterization of social medicine, its methods, the teaching of social medicine, and its meaning for the community and the individual. This section should be obligatory reading for every student of medicine, whether graduate or undergraduate.

Illustrative of the growing interest in social medicine and in the patient not as a "case" or a "specimen" but rather as a human being are the two volumes by Ryle and Clark-Kennedy. Dr. Ryle's book is a second edition of a volume originally published in 1936. The main preoccupation of this book is the natural history of disease in the individual. Indicative, however, of the change that has occurred in the intervening twelve years is Dr. Ryle's emphasis that the "natural history of disease in the community is a subject at least as worthy of attention," and the addition of a new chapter on the social pathology of rheumatic

fever. Dr. Clark-Kennedy undertakes to write a new kind of medical textbook, based on the patient as a person endowed with a certain heredity and living in a given environment. In this sense he defines pathology as "the study of the interaction between the genetic endowment of man, his way of life, and the environment into which he has been born." There is no doubt that this is a corrective long overdue in medical thinking and one that is needed if we are to develop a medicine suited to the complex society in which we live.

GEORGE ROSEN

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